

Fabrication of Silicon Out-of-Plane Microneedles for Potential Drug Delivery and Interstitial Fluid Extraction

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

Abstract

Microneedles represent a successful application of MEMS technology, forming minimally invasive platforms for transdermal drug delivery, body fluid sampling, and diagnostics. Silicon microneedles, in particular, are favored due to their exceptional mechanical strength and biocompatibility. This thesis focuses on the three different fabrication methods of silicon microneedles using MEMS techniques.

Initially, we fabricated silicon out-of-plane cone-shaped hollow microneedles with sharp apexes and off-axis pores. This process involved backside hole etching and frontside pillar etching via the Bosch process, followed by pillar sharpening using a HF-HNO₃ mixed solution. The resulting microneedles were 160 μm high. However, to penetrate the epidermis and access abundant body fluids for health monitoring systems, taller microneedles longer than 500 μm are required. Fabricating these higher microneedles proved challenging due to difficulties in achieving uniform sharpening through wet etching.

To address this, we developed a novel method for fabricating silicon out-of-plane hollow microneedles with beveled tips. This method included frontside slope etching, backside hole etching, and frontside pillar etching, combining anisotropic wet etching and dry etching (Bosch process). The resulting microneedles were approximately 600 μm tall with beveled sharp tips. We tested various fundamental functions of these microneedles by connecting the chip to a syringe using a 3D-printed applicator, successfully demonstrating liquid extraction, liquid injection, and simulated drug delivery process.

To minimize the impact of inevitable lateral etching during frontside pillar etching in the Bosch process, we proposed sacrificial structures surrounding the pillars to shield them from lateral etching. Testing two types of sacrificial structures, we found both structures could effectively reduce lateral etching, enabling the fabrication of 370 μm high ring pillars with vertical sidewalls.

Additionally, grayscale lithography combined with subsequent Bosch processing

presents an effective and flexible method for fabricating complex 3D structures like bevels. We first acquired contrast curve for the photoresist before grayscale lithography. Then we used this technique integrating frontside slope etching and frontside pillar etching into a single step, resulting in the fabrication of hollow microneedles measuring 325 μm in height.

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Dedication

For my family.

Table of Contents

Examining Committee Membership	ii
Author's Declaration	iii
Abstract.....	iv
Acknowledgements	vi
Dedication	xiv
List of Figures	xviii
List of Tables.....	xxvi
List of Abbreviations	xxviii
Chapter 1 Introduction to microneedles	1
1.1 Introduction to Micro/nano-fabrication and MEMS	1
1.2 Introduction to microneedles	4
1.2.1 Application of microneedles.....	5
1.2.2 Skin as the barrier.....	10
1.3 Classification of microneedles.....	12
1.3.1 In-plane microneedles and out-of-plane microneedles	12
1.3.2 Solid microneedles and hollow microneedles.....	13
1.3.3 Different materials of microneedles.....	23
1.4 Critical parameters of microneedles.....	24
Chapter 2 Specific microfabrication techniques for microneedle fabrication.....	25
2.1 Thin film deposition	25
2.2 Thermal oxidation.....	27
2.3 Photolithography	28
2.4 Etching.....	31
2.4.1 Wet etching	34
2.4.2 Dry etching.....	45
Chapter 3 Fabrication of silicon out-of-plane hollow microneedles by DRIE and HF-HNO ₃ sharpening.....	51

3.1 Overall design of silicon out-of-plane cone-shaped microneedles with sharp apex and off-axis pore.....	51
3.2 Backside hole etching	52
3.3 Frontside pillar etching	56
3.4 Wet etching sharpening.....	56
Chapter 4 Fabrication of silicon out-of-plane hollow microneedles by DRIE and KOH etching	60
4.1 Overall design of silicon out-of-plane microneedles with beveled sharp tip	60
4.2 Slope fabrication.....	63
4.2.1 Dry isotropic etching of the slope	63
4.2.2 Wet anisotropic etching of the slope	65
4.3 Backside hole etching	75
4.4 Frontside lithography	78
4.5 Frontside pillar etching	82
4.5.1 Frontside pillar etching optimization: sacrificial structures.....	85
4.6 Completed silicon hollow microneedles.....	97
4.7 Test of the microneedles.....	100
4.7.1 Extraction test	101
4.7.2 Injection test	102
4.7.3 Drug delivery test.....	103
4.7.4 Mechanical test	105
Chapter 5 Fabrication of silicon out-of-plane hollow microneedles by DRIE and grayscale lithography.....	110
5.1 Overall design of silicon out-of-plane microneedles with beveled sharp tip by grayscale lithography and DRIE	110
5.2 Backside hole etching	111
5.3 Grayscale lithography	113
5.3.1 Contrast curve measurement.....	113
5.3.2 Frontside patterning by grayscale lithography	114
5.4 Frontside pillar etching	117

Chapter 6 Conclusion and future work	122
6.1 Comparison of our fabrication process with the work from prior art.....	122
6.2 Conclusion and future work.....	125
6.3 List of Publications.....	126
References.....	128

List of Figures

Figure 1.1 Schematic diagram of (a) Top-down and (b) bottom-up approaches.	2
Figure 1.2 Roadmap of feature size in semiconductor devices for TSMC.....	3
Figure 1.3 Skin anatomy and schematics of microneedles for drug delivery.	5
Figure 1.4 Comparison of topical cream, hypodermic needle, microneedle patch and transdermal patch.	6
Figure 1.5 Examples of application of microneedles in transdermal drug delivery. (a) A glucose-responsive insulin patch for regulating blood glucose; (b) A porous microneedle array patch based on transdermal electroosmosis; (c) A Patch with thermal responsive microneedles for monitoring and treatment of diabetes; (d) The microneedle platform for buccal macromolecule transportation; (e) A rapidly detachable microneedle patch for continuous release of contraceptives.	7
Figure 1.6 Illustration of the blood collection and interstitial fluid extraction devices. (a) An elastic self-healing actuator integrated with microneedles for blood collection; (b) A hydrogel microneedle patch for detecting interstitial fluid; (c) The hydrogel patch is integrated with an electronic glucose sensor for rapid extraction of microliter skin interstitial fluid; (d) A microneedle patch based on plasma paper for molecular detection in dermal interstitial fluid; (e) The 3D printing device for interstitial fluid extraction with inclined microneedle penetration.	8
Figure 1.7 Examples of wearable microneedle-based biosensor. (a) A diabetes sensor patch based on hollow biodegradable microneedles; (b) A bioimpedance sensor based on microneedle for precision farming; (c) An extended gate transistor based on wearable microneedles for real-time detection of sodium in interstitial fluid; (d) A wearable patch using ion electrophoresis double extraction for rapid capture and detection of Epstein Barr virus cell-free DNA.	10
Figure 1.8 Schematic of the fluid-filled space supported by a network of collagen bundles lined on one side with cells.....	12
Figure 1.9 Out-of-plane and in-plane microneedles. (a) 350 μm high, sharpened 2D	

silicon microneedle array; (b) 1.2 mm long silicon in-plane microneedles with microchannels.	13
Figure 1.10 (a) Solid silicon microneedles used for transdermal drug delivery. Approximately 80 μm at the base and 150 μm long solid microneedles were fabricated in silicon using DRIE, and featured sharp tips with a tip radius below 1 μm . (b) The first hollow out-of-plane microneedles by McAllister et al. The silicon needles are 150 μm long and were fabricated through DRIE using Bosch process.	14
Figure 1.11 Schematic of process flow for the fabrication of silicon out-of-plane microneedles.	15
Figure 1.12 Hollow silicon microneedles by Stoeber and Liepmann. The 200 μm long needles are fabricated by Bosch DRIE and sharpened by isotropic dry etching. (a) Pointed tip; (b) Flat tip.	15
Figure 1.13 210 μm high, cross-shaped, hollow, side-opened, silicon microneedles fabricated by Griss and Stemme. (a) Needles with a 50 μm long base shaft. (b) Needles without a base shaft.	16
Figure 1.14 Process flow for the fabrication of circular side-opened hollow microneedles.	17
Figure 1.15 The circular side-opened design developed by Roxhed et al. (a) 400 μm long, ultra-sharp, side-opened microneedles. (b) Magnified view of the microneedle tip. The tip-radius is below 100 nm.	18
Figure 1.16 Fabrication process for microneedle using DRIE and KOH wet etching. Left, cross-sectional drawing of the sample at dotted line; Right, top view of the process.	19
Figure 1.17 (a) SEM micrograph of a 350 μm high microneedle, with a base of 250 μm . (b) SEM picture of a microneedle with a tip having large radius of curvature.	20
Figure 1.18 Fabrication process for microneedles using the combination of KOH wet etching and Bosch process.	21
Figure 1.19 SEM image of a 500 μm tall microneedles with a 50- μm diameter offset pore.	22
Figure 1.20 Examples of microneedles in different materials. (a) Silicon; (b) Glass; (c)	

Ormocer; (d) Glassy carbon; (e) Steel; (f) Polyvinylpyrrolidone; (g) Polylactide; (h) Polyvinylalcohol; (i) Polypropylene.	23
Figure 2.1 Overview of thin film growth on substrate surface in chemical vapor deposition.....	26
Figure 2.2 Diagram of PECVD reactor, here using a high density ECR (electron-cyclotron resonance) plasma source instead of the more popular parallel-plate plasma source.	27
Figure 2.3 Nabertherm muffle furnace up to 1100 °C (Courtesy to Nabertherm).	27
Figure 2.4 MA/BA6 Mask and Bond Aligner (Courtesy to SUSS MicroTec).	29
Figure 2.5 (a) Heidelberg DWL 66+ laser lithography system. (b) The principle of SLM in Heidelberg Direct Write Lithography system.	30
Figure 2.6 Basic photolithography process using positive photoresist: the exposure and etching process that allows one to transfer a pattern to the film/wafer.	31
Figure 2.7 Silicon etch rates in ($\mu\text{m}/\text{h}$) for various KOH concentrations and etch temperatures.	32
Figure 2.8 A graphical representation of (a) a poor selectivity that causes the etchant to attack the bottom layer material while removing the top layer, (b) a high selectivity that results in etching out the top layer without affecting the underlying layer.	33
Figure 2.9 A schematic of (a) isotropic etching of silicon (b) partially anisotropic (c) completely anisotropic.	33
Figure 2.10 A schematic of wet etching process: (1) the diffusion of the reactants to the reacting surfaces, (2) the chemical reaction at the surface, (3) the transportation of the products away from the surface via liquid flow.	34
Figure 2.11 A graphical representation of silicon crystal planes.	35
Figure 2.12 Silicon bulk profile after KOH etching. (a) Schematic diagram of cross-section of (100) oriented silicon etched by KOH solution. (b) SEM image of KOH etched (110) oriented silicon with line pattern. (c) SEM image of KOH etched (100) oriented silicon with square pattern.	36
Figure 2.13 (100) Si etch rate vs. the temperature for 30% KOH solution.	37
Figure 2.14 Etch rate of the (100) silicon crystal plane as a function of KOH	

concentration at 72 °C.	38
Figure 2.15 Etch rates of silicon oxide in (a) TMAH and (b) KOH.	39
Figure 2.16 Etch rates of (100) and (110) Si surfaces in 3M and 5M KOH solution vs. alcohol concentrations.	40
Figure 2.17 Schematic illustration of adsorption of surface active compound molecules like IPA and Triton X-100 on the (110) surface during silicon anisotropic etching in alkaline solution. The molecules adsorb with their hydrocarbon chains.	41
Figure 2.18 Wet etch process flow proposed by Wilke et al.	42
Figure 2.19 SEM micrographs of a single microneedle fabricated by Wilke et al.. Left, side view of the needle with a small negative top; middle, side view; right, top view.	42
Figure 2.20 Curves of constant etch rate of silicon (mils/min) as a function of etchant composition in the system 49.25% HF, 69.51% HNO ₃ , and diluent.	44
Figure 2.21 SEM images showing progress of needle formation from dicing through etching (a–f). The rectangular columns (a) are transformed into sharp needle shapes (d) during static etching (8 min). The high etch rate (20 μm/min) causes change in the geometry.	45
Figure 2.22 Typical etching profiles of the three basic mechanisms of dry plasma etching. (a) the chemical plasma etching (PE), (b) the synergetic reactive ion etching (RIE) and (c) the physical ion beam etching (IBE).	46
Figure 2.23 Etch rates of silicon as only XeF ₂ gas (pure chemical etching, without plasma), only Argon ion beam (pure physical etching), and combination of them are introduced to the silicon surface. Ion-assisted chemical etch undoubtedly boosts the efficiency of the etching.	47
Figure 2.24 Reaction steps of RIE for the case of silicon etching.	48
Figure 2.25 Bosch process and the alternation between the passivation and etching step.	50
Figure 2.26 Etch rate curve related to the amount of exposed silicon.	50
Figure 3.1 Schematic fabrication processing of hollow silicon microneedle arrays. (a) Backside resist coating; (b) Backside lithography; (c) DRIE on the backside for hole	

etching; (d) Lithography via backside alignment; (e) DRIE on the frontside for pillar etching; (f) Wet etch sharpening.	52
Figure 3.2 (a) ARDE lag exhibited in typical plasma etch process. The final etch depths in wider trenches are larger. (b) A plot of trench depth normalized to that of a 100- μm -wide trench. An $\sim 50\%$ ARDE lag is observed in a 2.5- μm -wide trench. (c) A plot of the connection between etch rate and aspect ratio according to the tests in Oxford PlasmaPro Cobra 100 in CIRFE Lab. A 70% decrease in the etch rate was observed when the aspect ratio was changed from 0 to 6.	53
Figure 3.3 The optimization of hole DRIE etching using triple-phase modified Bosch processing.	55
Figure 3.4 Pillar etching using standard Bosch process. (a) 300 cycles; (b) 900 cycles.	56
Figure 3.5 (a) SEM image for a solid silicon microneedles array with high uniformity; (b) the zoomed-in view of an individual sharp needle.	57
Figure 3.6 Hollow microneedles sharpened by wet etching.	58
Figure 3.7 SEM micrograph of silicon out-of-plane microneedle after HF and HNO_3 mixed solution wet sharpening. The height is about 300 μm	59
Figure 4.1 Design of the microneedle mask pattern. (a) Frontside rectangle design to fabricate the slope, the width of the rectangle is 400 μm and the length is 1.5 cm, and the gap is 1000 μm ; (b) Backside design of the microneedles, the diameter of the holes is 80-100 μm ; (c) Frontside design of the microneedles, the outer diameter of the rings is 200-240 μm and the inner diameter is 80-100 μm	62
Figure 4.2 Schematic fabrication processing of hollow silicon microneedle arrays. (a) Silicon nitride coating on both sides and frontside resist coating; (b) Photolithography on the frontside and pattern transfer via silicon nitride etching; (c) Isotropic wet etching on the front side; (d) Backside resist coating and photolithography via backside alignment; (e) DRIE on the backside; (f) Second frontside pattern on the slopes; (g) DRIE on the frontside; (h) Final schematic of the microneedle array.	62
Figure 4.3 Cross-sectional SEM image of the slope after 50 minutes' SF_6 Etch. The wafer is 500 μm thick and slope is 200 μm high.	65

Figure 4.4 Cross-sectional SEM image of the slope after 2.5 h KOH wet etch. The slope is 250 μm high and 200 μm wide, showing a 54.7° slope.	68
Figure 4.5 Phase separation of KOH-IPA saturated solution.	69
Figure 4.6 Cross-sectional SEM image of 45° slope after 2 h wet etching by KOH with saturated IPA.	70
Figure 4.7 SEM image of 45° slope after 4 h wet etching by KOH with saturated IPA.	71
Figure 4.8 Image of the sample after 4 h wet etch using KOH with saturated IPA. ..	71
Figure 4.9 Cross-sectional SEM image of 54.7° slope fabricated by TMAH with Triton X-100.	73
Figure 4.10 Cross-sectional SEM image of 45° slope fabricated by TMAH with Triton X-100.	74
Figure 4.11 SEM image for the holes (a) after 700 cycles of Standard Bosch recipe, the depth is 320 μm , the diameter is 60 μm ; (b) after 700 cycles of Standard Bosch recipe and 600 cycles of Revised Bosch recipe, the depth is 320 μm and the diameter is 60 μm	76
Figure 4.12 SEM image of the holes after DRIE in Zhejiang University. The depth is about 500 μm and the diameter is 80 μm	78
Figure 4.13 Profile of spin-coated photoresist (HTF-4025G, Hantop, China) after frontside photolithography.	79
Figure 4.14 Cross-sectional microscopy image of 54.7° slope with spray coated SUN-9i negative photoresist.	80
Figure 4.15 Frontside alignment during frontside photolithography on the slope.	81
Figure 4.16 Frontside ring structures after photolithography on 54.7° slope using SUN-9i photoresist. (a) Top view of microscopy image of ring structures; (b) SEM image of ring structures.	82
Figure 4.17 Frontside ring structures after photolithography on 45° using ROL-7133 photoresist. (a) Top view of microscopy image of ring structures; (b) SEM image of ring structures.	82
Figure 4.18 SEM photograph for etched pillars. (a) Pillars etched via standard Bosch	

recipe in Quantum NanoFab, the height is 297 μm with apparent negative tapered profile. (b) Pillars etched via Bosch Processing in Oxford PlasmaPro100 ICP-350, the height is 200 μm with apparent negative tapered profile.	83
Figure 4.19 An example of lateral etching during DRIE for etching widely-spaced micro-pillars.	87
Figure 4.20 Design of the sacrificial structures. (a) sideview of the etching process with and without sacrificial structures; (i)-(iii) without sacrificial structures; (iv)-(vi) with sacrificial structures; (b) one full circle structure; (c) two half-circle structure, other dimensions in (c) are same as (b), the shadowed parts are covered by etch mask.	89
Figure 4.21 Microscopy images of ring pillar and sacrificial structure patterns after photolithography. (a) one full circle structure; (b) two half-circle structure.	90
Figure 4.22 Pillar structures etched without sacrificial structures.	92
Figure 4.23 Silicon pillars etched with circular sacrificial structures. (a) Top view of pillars with circular sacrificial structures; (b) Top view of pillars with broken off circular sacrificial structures after ultrasonic agitation; (c) Sideview of pillars with circular sacrificial structures after ultrasonic agitation; (d) Side view of pillars with sacrificial structures collapsed before the end of etching, without ultrasonic agitation.	93
Figure 4.24 The hollow silicon pillars etched with two half-circle sacrificial structures. (a) Top view of pillars with sacrificial structures after 1600 cycles of Bosch process; (b) Top view of pillars after 1800 cycles of Bosch process; (c) Sideview of a pillar with sacrificial structures after 1600 cycles of Bosch process; (d) Sideview of a pillar after 1800 cycles of Bosch process; (e) Sideview of pillars, showing the etching local uniformity; (f) Sideview of hole structures at the center of pillars.	96
Figure 4.25 Completed microneedle chip.	98
Figure 4.26 SEM images of microneedles with 54.7° slope.	99
Figure 4.27 SEM images of microneedles with 45° slope.	99
Figure 4.28 Microneedle test device manufacturing. (a) Polymer applicator fabricated by 3D printing; (b) Microneedle chip connecting syringe with applicator.	101
Figure 4.29 Capillary filling and microneedle extraction of blue ink.	102
Figure 4.30 Water injection through microneedle.	103

Figure 4.31 Microneedle penetrations into porcine skin.	104
Figure 4.32 (a) Original and (b) microscopy image of the porcine skin after blue ink delivery.	105
Figure 4.33 Instron 5548 micro tester. The microneedle chip is placed on the platform (circled area).	106
Figure 4.34 Microneedle chip after mechanical test with all the needles collapsed.	107
Figure 4.35 Force-displacement form for sample 1.	108
Figure 5.1 Process flow of microneedle fabrication based on grayscale lithography. (a) Backside hole etching; (b) Grayscale lithography to form slope-shape rings; (c) Frontside pillar etching.	111
Figure 5.2 SEM image of through-holes with 400 μm deep and a diameter of 80 μm . (a) Top view of holes array; (b) Top view close-up image; (c) Cross-sectional image of the hole; (d) Cross-sectional close-up image.	113
Figure 5.3 Contrast curve of remaining height of photoresist (SUN-9i) and laser power.	114
Figure 5.4 Pattern design of gray-scale lithography mask and outline after exposure and development.	116
Figure 5.5 SEM image of ring structure obtained by grayscale lithography. The inner diameter of the ring is 80 μm and the outer diameter is 200 μm . (a) Top view of photoresist profile; (b) Top view close-up image.	116
Figure 5.6 SEM image of etching results of microneedles after Bosch process.	118
Figure 5.7 Morphology of microneedle optimized by SF ₆ etching.	119
Figure 5.8 Photoresist mask structure after thermal reflow treatment. (a) Scanning electron microscope image of photoresist structure; (b) Photoresist profile after thermal reflow.	120
Figure 5.9 SEM image of microneedles after (a) Bosch process and (b) SF ₆ etching subsequently.	120

List of Tables

Table 1.1 Advantages and disadvantages of each type of microneedle system for drug delivery.	9
Table 3.1 Parameters of DRIE etching process with an RF frequency of 13.56 MHz.	54
Table 4.1 Parameters of the SF6 only isotropic etching process with an RF frequency of 13.56 MHz.	64
Table 4.2 Parameters of PECVD of silicon nitride deposition.....	66
Table 4.3 Parameter of ICP-RIE for silicon nitride etching.	67
Table 4.4 Summary of four different wet etching methods to fabricate slope.	74
Table 4.5 Parameters of the Standard Bosch Process recipe for hole etching on Oxford PlasmaPro Cobra 100 in CIRFE Lab (Bosch process) with an RF frequency of 13.56 MHz at 0 °C.	76
Table 4.6 Parameters of the Revised Bosch Process recipe for hole etching on Oxford PlasmaPro Cobra 100 in CIRFE Lab (Bosch process) with an RF frequency of 13.56 MHz at 0 °C.	76
Table 4.7 Parameters of the DRIE etching process for backside hole etching (Bosch process) with an RF frequency of 13.56 MHz at 15 °C.	77
Table 4.8 Parameters of the DRIE high rate etching process on Oxford Estrelas 100 with an RF frequency of 13.56 MHz at 5 °C.	84
Table 4.9 Parameters of the DRIE etching process on Samco RIE-iPB800 with an RF frequency of 13.56 MHz at -10 °C.	84
Table 4.10 Parameters of the DRIE etching process (Bosch Process) with an RF frequency of 13.56 MHz at 15 °C.	90
Table 4.11 Max total force and max average force on each needle for all samples. .	108
Table 5.1 Parameters of the DRIE etching process on Samco RIE-iPB800 for backside hole etching (Bosch process) with an RF frequency of 13.56 MHz at -10 °C.	111
Table 5.2 Exposure power of each layer in grayscale photolithography.	115

Table 5.3 Parameters of the DRIE etching process on Samco RIE-iPB800 for frontside pillar etching (Bosch process) with an RF frequency of 13.56 MHz at -10 °C.	117
Table 5.4 Parameters of SF6 etching process on Samco RIE-iPB800.	119
Table 6.1 Comparison of parameters of microneedles fabricated by our fabrication process with the microneedle fabrication process by the work from prior art.	123

List of Abbreviations

MEMS Microelectromechanical system

UV Ultraviolet

DRIE Deep reactive ion etching

ARDE Aspect ratio dependent etching

Chapter 1

Introduction to microneedles

This chapter introduces the concept of micro/nanofabrication and microelectromechanical systems (MEMS). Additionally, it provides an overview of microneedles, encompassing their various applications, classifications, and critical parameters.

1.1 Introduction to Micro/nano-fabrication and MEMS

On December 29, 1959, Dr. Richard P. Feynman gave a talk at the annual meeting of the American Physical Society at Caltech named “There’s Plenty Room at the Bottom, an Invitation to Enter a New Field of Physics”, showing that we can decrease the size of the things in practice and we can achieve a lot through that including information on a small scale, marvelous biological system, and miniaturizing the computer¹. Over a decade later, Japanese scientist Norio Taniguchi from Tokyo University of Science first coined the concept of “nanotechnology”. The fundamental basis of nanotechnology is making functional materials, devices, and systems on the nanometer length scale. Nanoparticles (NPs) are defined as ultrafine particles sized between 1 and 100 nm in diameter, where unique phenomena enable novel applications². In 1982, Binnig and Rohrer in IBM invented scanning tunneling microscope³, representing the beginning of the high-speed development of modern nanotechnology.

Nowadays, nanotechnology is a highly cross-disciplinary subject involving the theory of physics, chemistry, biology, pharmacy, and material science and engineering. Owing to the development of nanotechnology, there are wide applications such as Integrated

Circuit (IC), Microelectromechanical System (MEMS), photovoltaic device, nanotube / wire, micro-optics and so on.

Nanofabrication is the manufacturing of structures and devices with dimensions on nanometer scale. “Top-down” and “Bottom-up” are two fundamental conceptional approaches to fabricate nanostructure^{4,5}. Top-down approach begins with the patterns on large scale and creates nanoscale pattern on substrate materials by lithography and etching, while bottom-up approach forms nanoscale structure starting from assembling atoms, molecules, clusters or other subunits into larger structures, with the help of chemical or physical forces such as surface tension, electrostatic force and hydrophobic-hydrophilic interactions. Top-down approach is good for producing structures with long-range order and making macroscopic connections, whereas bottom-up approach is best suited for self-assembly and establishing short-range order at the nanoscale.

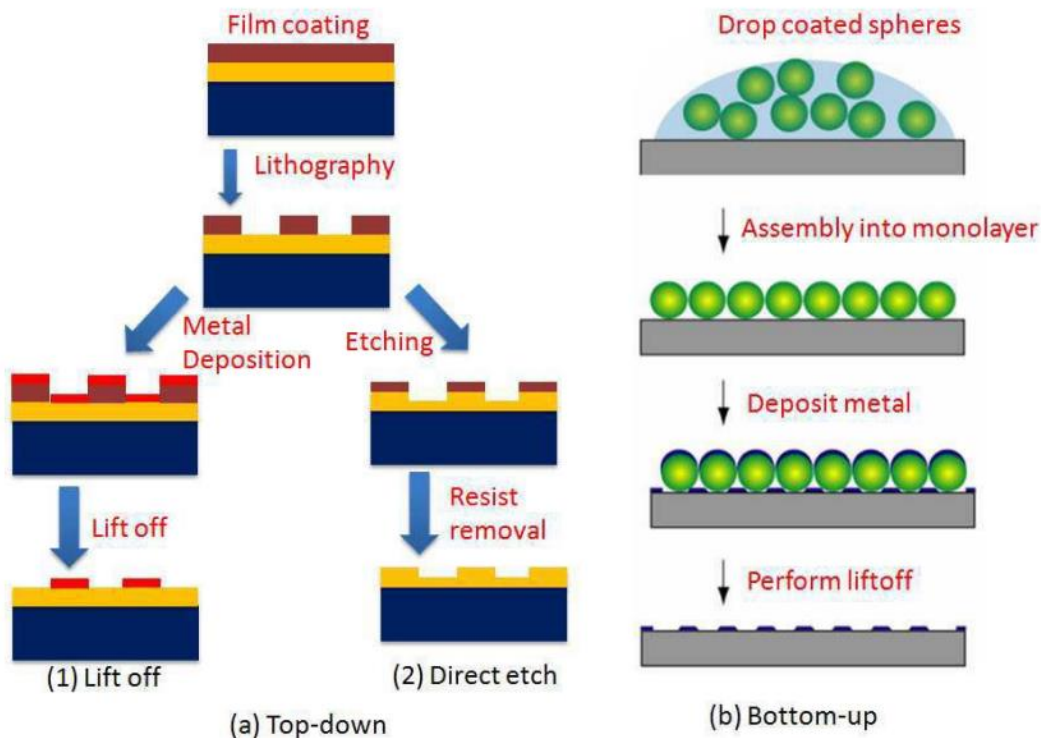


Figure 1.1 Schematic diagram of (a) Top-down and (b) bottom-up approaches⁶.

Since 2000, demand for IC products has increased dramatically. Consequently, the top-down approach, which involves photo-lithographic patterning techniques, has become more and more popular in modern IC production. By using a light source with a lower wavelength, an exponentially decreasing feature size of the IC product has been achieved in decades. Figure 1.2 shows the roadmap of technology nodes for semiconductors by year. The light source plays an important role in determining the resolution of photolithography. Since 1980s, the lithography light sources have been developed from ultraviolet (UV) generated by a mercury vapor lamp (g-line=436nm, h-line=405nm, i-line=365nm) to deep UV generated by an excimer laser (KrF=248nm, ArF=193nm). Extreme UV (EUV) generated by laser-pulsed tin plasma with a wavelength of 13.5nm is considered as state-of-the-art lithography technology. The miniaturization of IC-related devices dramatically reduces the size, weight, and energy consumption of electronic devices, fundamentally supporting modern Internet technology and big data storage and analysis⁷.

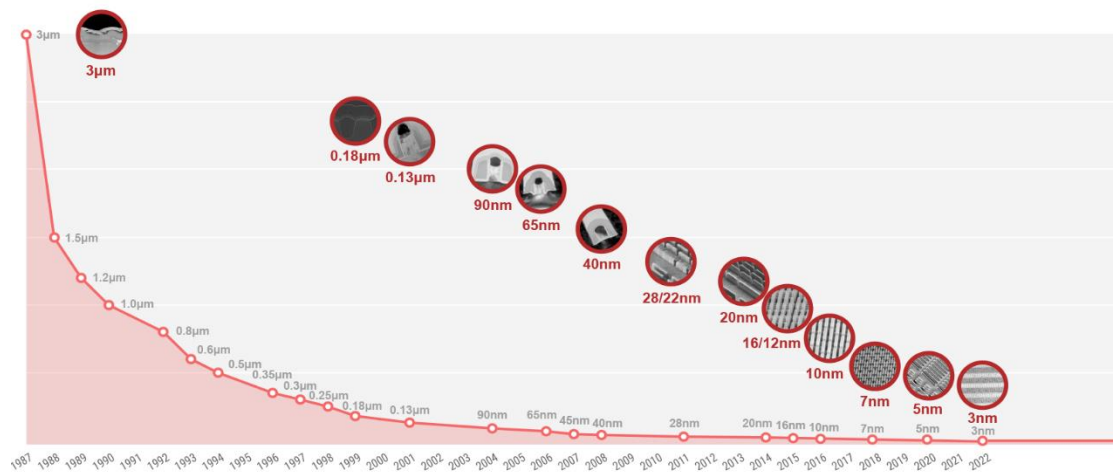


Figure 1.2 Roadmap of feature size in semiconductor devices for TSMC⁸.

Microelectromechanical systems (MEMS) are a group of miniature devices and systems fabricated using micromachining processes. MEMS innovation is a forerunner to the increasingly well-known and state-of-the-art technology in nanotechnology, which alludes to science, design and innovation from the micrometer scale to the atomic scale. Initially, MEMS were invented by the microfabrication techniques for a variety

of applications such as electronics, sensors, and actuators^{9,7,10}. MEMS devices have critical dimensions ranging from 100 nm to 1000 μm . Consequently, the small size of these devices can provide many advantages over large-scale systems in the aspects of power usage, sensitivity, cost, and space requirement. Initially, MEMS was based on silicon using bulk micromachining and surface micromachining processes¹¹. Gradually, other materials, for instance, polymers, metals and ceramics, are commonly applied in MEMS fabrication.

With the development of microtechnology, various functional MEMS applications have been developed in daily life. Finally, MEMS technology has established itself as a specialized field of study with a significant market share. As a unique, innovative product, MEMS devices have been merged with a variety of fields such as mechanics, fluidics, medical and healthcare. In this way, the field of BioMEMS has drawn numerous attentions¹². Miniaturized medical wearables and implants, transdermal drug delivery systems, on-chip assays, cell sorting devices, and DNA sequencers are some typical examples of BioMEMS. Similarly, as one of the typical biomedical applications, MEMS-based microneedles have been used for transdermal drug delivery, blood extraction and bodily fluid sampling. At present, solid or hollow microneedles using different materials with various shaft shapes are integrated and used in conjunction with microfluidic systems.

1.2 Introduction to microneedles

Microneedles are devices which are provided for the transport of therapeutic and biological molecules across tissue barriers and for use as microflameholders¹³. Microneedle technologies have recently become increasingly attractive for realizing minimally-invasive platforms capable of microfluidic neural probes for precise chemical neural stimulation^{14,15}, transdermal drug delivery^{16,17}, bodily fluid sampling¹⁸ and health monitoring systems¹⁹. Microneedles are anticipated to mitigate the

shortcomings associated with lancets and hypodermic needles^{20, 21, 22}. It is also anticipated that the capability of combining a fluid delivery channel with a neural recording array will have broad applications. For instance, in terms of drug delivery, oral delivery may inactivate some proteins, DNA, genes and antibodies, and most biomolecules cannot pass through the skin barrier due to their unfavorable hydrophilicity and macro size^{23, 24}. However, microneedles can overcome these drawbacks by penetrating the outermost layer. As shown in Figure 1.3, microneedles require only a small area of skin and enter at a limited depth, resulting in minimal irritation of the dermal layers associated with pain and tissue damage.

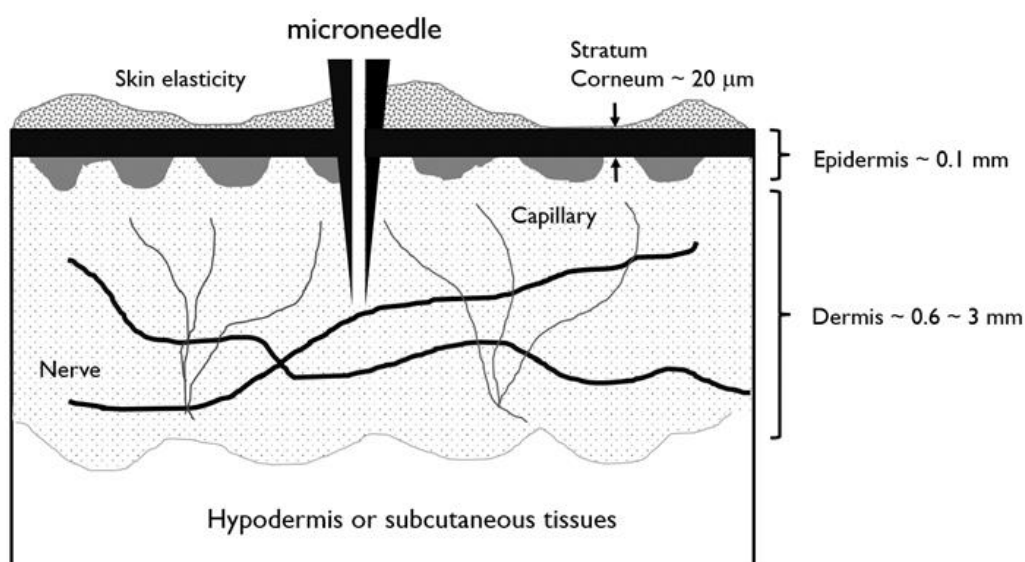


Figure 1.3 Skin anatomy and schematics of microneedles for drug delivery.

1.2.1 Application of microneedles

In the past, oral administration of drugs was considered a conventional and effective drug delivery method. However, some drawbacks have gradually emerged because oral administration is often not applicable to new protein-based, DNA-based, and other therapeutic compounds produced by modern biotechnology^{25, 26, 27}. Correspondingly,

applying transdermal patches to deliver drugs across the skin has gradually become a desired approach for patients who are suffering painful injections via a hypodermic needle. However, transdermal delivery, including topical cream (i.e. hand cream) and transdermal patch (i.e. BandAid), which rely on drugs passively diffusing across the skin, is severely restricted and hindered by the low permeability of the outer 10-20 μm of skin, the stratum corneum layer^{28,29}.

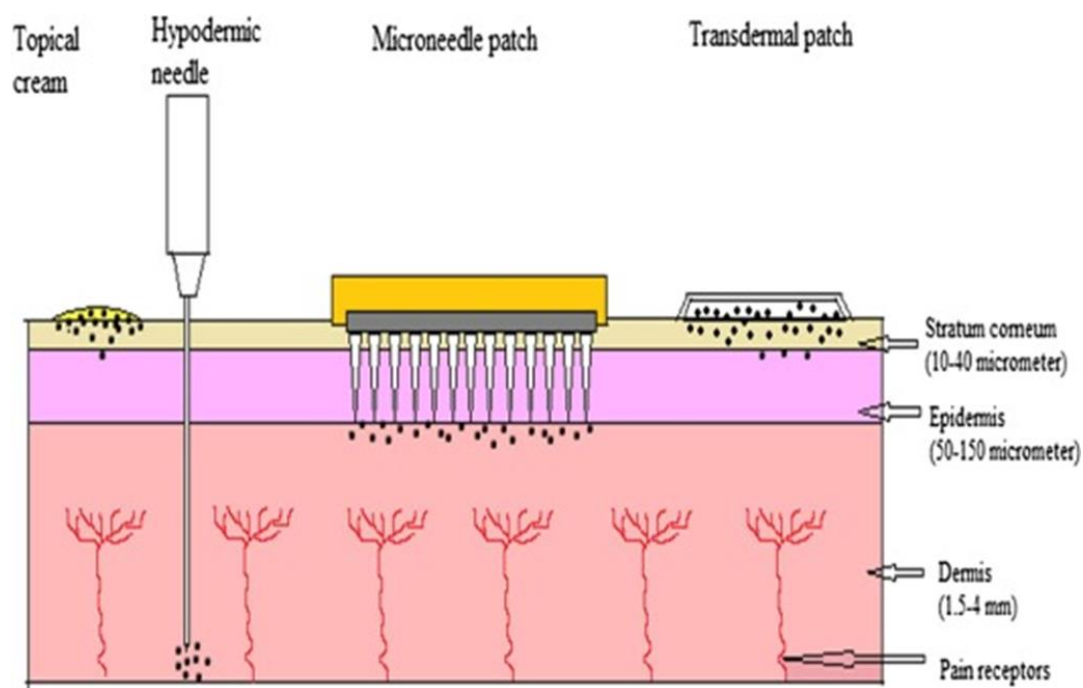


Figure 1.4 Comparison of topical cream, hypodermic needle, microneedle patch and transdermal patch³⁰.

To increase skin permeability and reduce pain simultaneously, the idea of combining the benefits of needle injection and transdermal patches is introduced, resulting in the creation of the microneedle concept (Figure 1.4). This concept involves micron-sized needles with representative parts that are generally hundreds of microns long, few to tens of microns wide at the tip, and on the order of 100 μm wide at the base³¹. Such microneedles are sufficiently long to penetrate the outer layer of the skin without interfering with the nerve endings in the deeper layer, enabling minimally invasive and

painless sampling, showing superiority in drug delivery (Figure 1.5). In contrast to drug injection, microneedles can also be used to extract the interstitial fluid (Figure 1.6).

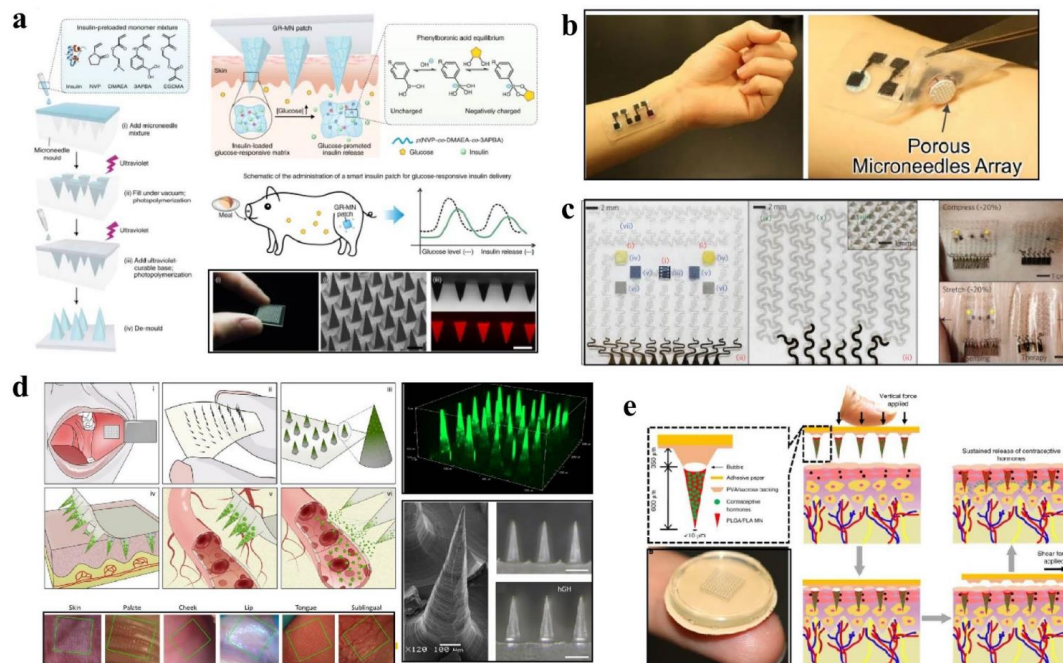


Figure 1.5 Examples of application of microneedles in transdermal drug delivery³². (a) A glucose-responsive insulin patch for regulating blood glucose³³; (b) A porous microneedle array patch based on transdermal electroosmosis³⁴; (c) A Patch with thermal responsive microneedles for monitoring and treatment of diabetes³⁵; (d) The microneedle platform for buccal macromolecule transportation³⁶; (e) A rapidly detachable microneedle patch for continuous release of contraceptives³⁷

To achieve drug delivery, microneedle systems can be divided into five series. Table 1.1 lists the advantages and disadvantages for all five types of microneedle systems. The first type is the solid microneedle, which can be used for efficient pretreatment. After insertion and removal of the microneedles, micron-sized holes are formed on the skin surface, and the drug formulation can be applied to the skin, allowing the drug to slowly diffuse through the holes and into the body³⁸. In the second method, the drug is coated onto the surface of the microneedles, and after insertion, the drug remains in the tissue. The third method is dissolving microneedles, which are typically formed by

polymers. The drug is pre-dissolved in the microneedles, and after insertion, the whole microneedles remain in the skin for dissolution. The fourth method involves hollow microneedles, whose drug delivery concept is similar to that of typical hypodermic needles. The drug passes through the hole in the needle and passes through the skin. The fifth method uses hydrogel-forming microneedle. The concept is also similar to that of hypodermic needles, but this type of microneedle is fabricated with some special materials that are available for drug to pass through.

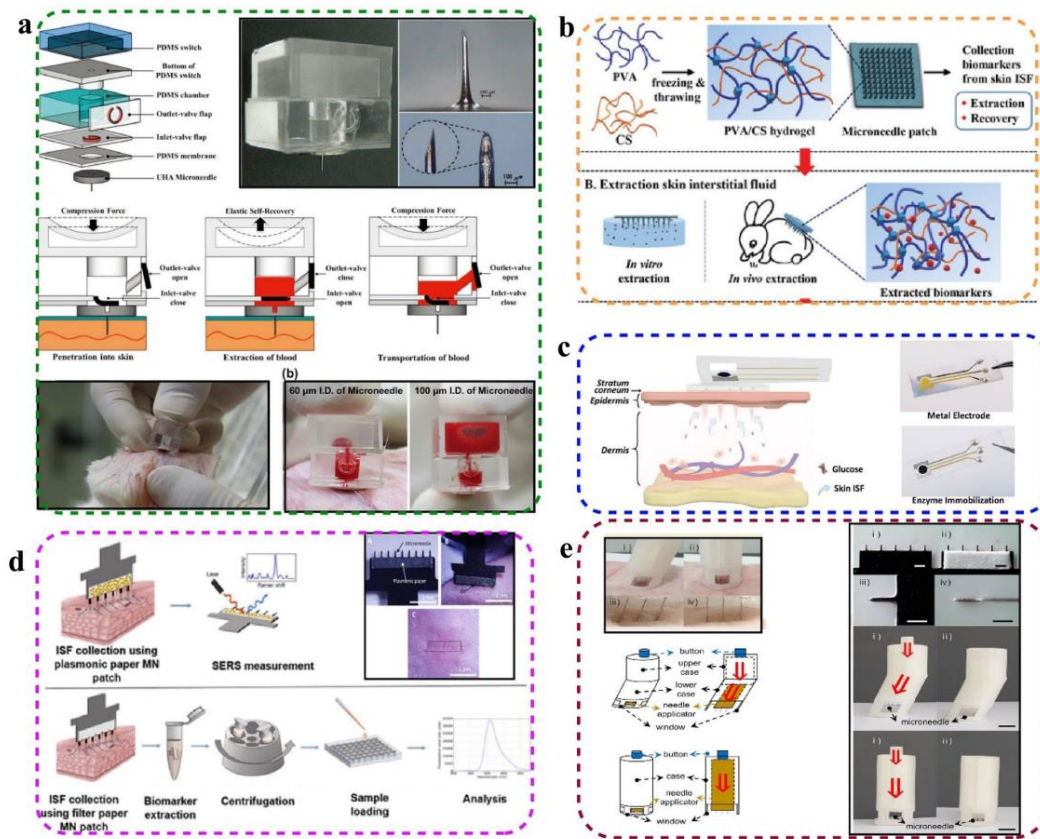
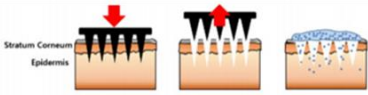
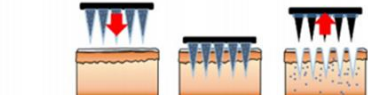
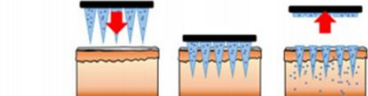
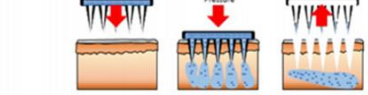
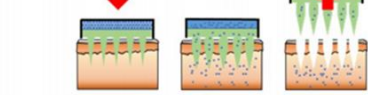


Figure 1.6 Illustration of the blood collection and interstitial fluid extraction devices³². (a) An elastic self-healing actuator integrated with microneedles for blood collection³⁹; (b) A hydrogel microneedle patch for detecting interstitial fluid⁴⁰; (c) The hydrogel patch is integrated with an electronic glucose sensor for rapid extraction of microliter skin interstitial fluid⁴¹; (d) A microneedle patch based on plasma paper for molecular detection in dermal interstitial fluid⁴²; (e) The 3D printing device for interstitial fluid extraction with inclined microneedle penetration⁴³.

Table 1.1 Advantages and disadvantages of each type of microneedle system for drug delivery⁴⁴.

Microneedle Type	Schematic illustration	Advantages	Disadvantages
Solid	 The diagram shows three stages: 1. Insertion of solid needles into the skin (labeled Stratum Corneum and Epidermis). 2. Dwell time where the needles are in the skin. 3. Removal of the needles, leaving channels in the skin.	Mechanical strength Physical stability Reasonable drug loading	Poor dose accuracy Requirements of rapid healing after application Potential for infection due to reuse Poor biocompatibility
Coated	 The diagram shows three stages: 1. Insertion of coated needles. 2. Dwell time where the needles are in the skin. 3. Removal of the needles, leaving the coating in the skin.	Mechanical strength	Peeling during insertion Poor biocompatibility Dose limitation Formulation migration during manufacturing and storage
Dissolving	 The diagram shows three stages: 1. Insertion of dissolving needles. 2. Dwell time where the needles are in the skin. 3. Removal of the needles, which dissolve into the skin.	Low-cost manufacturing Easy of manufacturing Controlled drug release profile One-step application	Poor mechanical strength, physical stability, and biocompatibility Dose limitation
Hollow	 The diagram shows three stages: 1. Insertion of hollow needles. 2. Dwell time where the needles are in the skin, with a 'Pressure' arrow indicating fluid flow. 3. Removal of the needles, leaving channels in the skin.	Dose accuracy Reasonable drug loading Constant flow rate	Clogging Ingressing body fluids Requirement of prefilled syringe Poor mechanical strength Potential for infection due to reuse Poor biocompatibility
Hydrogel-forming	 The diagram shows three stages: 1. Insertion of hydrogel-forming needles. 2. Dwell time where the needles are in the skin. 3. Removal of the needles, which form a hydrogel in the skin.	No residual excipients in the skin after removal Easy to manufacture Reasonable drug loading Controlled drug release profile	Poor mechanical strength and physical stability Ingressing body fluids

In addition to drug delivery, microneedles play an important role in biosensing. The structures of microneedles allow them to function as sensors or sensor carriers to achieve in vivo sensing of biomarkers such as glucose, DNA and proteins. Moreover, because the height of the microneedles is not too long to become painful, wearable devices based on microneedles are desired, making it possible to continuously monitor biomarkers in interstitial fluid.

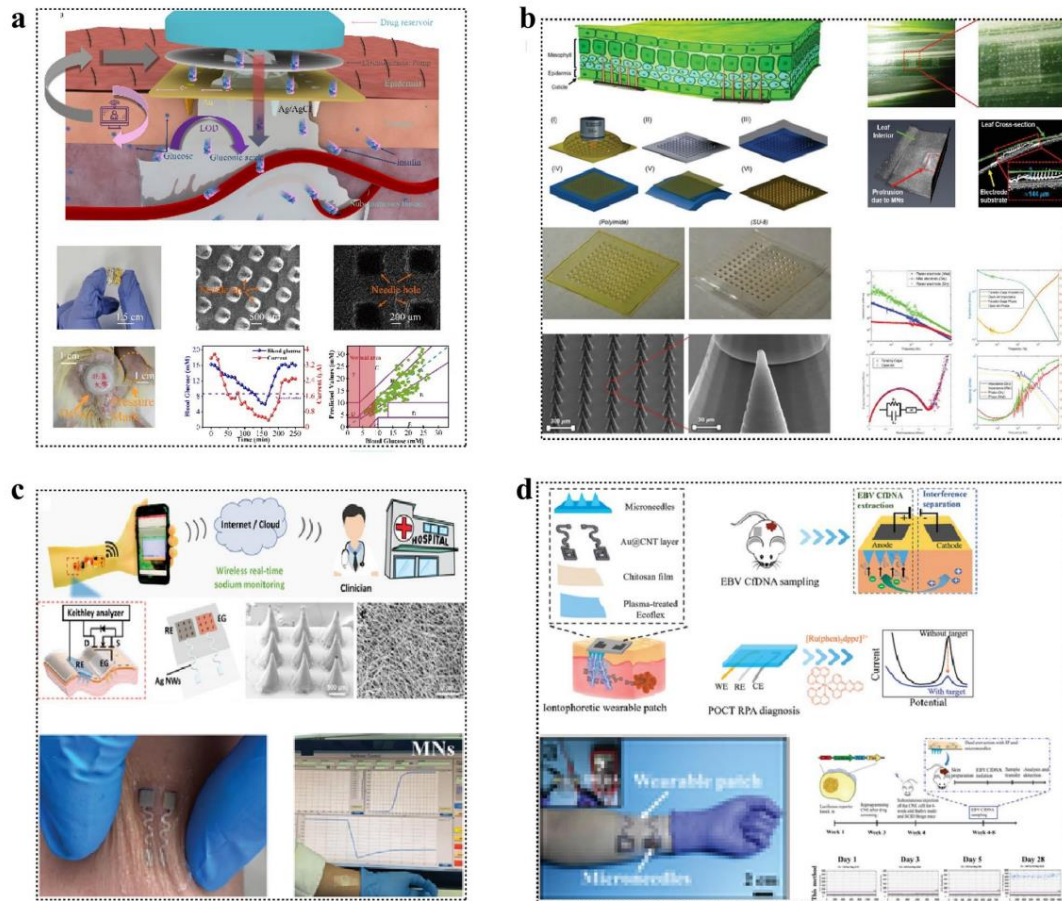


Figure 1.7 Examples of wearable microneedle-based biosensor³². (a) A diabetes sensor patch based on hollow biodegradable microneedles⁴⁵; (b) A bioimpedance sensor based on microneedle for precision farming⁴⁶; (c) An extended gate transistor based on wearable microneedles for real-time detection of sodium in interstitial fluid⁴⁷; (d) A wearable patch using ion electrophoresis double extraction for rapid capture and detection of Epstein Barr virus cell-free DNA⁴⁸.

1.2.2 Skin as the barrier

The skin is the largest organ of the body covering approximately 20 square feet. The skin protects us from the entry of foreign elements and the loss of water and heat from the body. This is also a critical route for drug delivery and biofluid extraction. Human skin can be categorized into three primary layers: the top layer is the epidermis, the

layer underneath that is the dermis, and the deepest layer is the hypodermis. The epidermis layer is optimally targeted for interstitial fluid extraction and is superficial enough to be painless. The thickness of the epidermis layer is approximately 50-150 μm , but the thickest part could be even 1500 μm ¹⁸. The epidermis can be divided into two parts: stratum corneum and stratum spinosum. The outermost layer of the epidermis is the stratum corneum, consisting of adherent dead, cornified cells, and varying in thickness from 10-40 μm . The epidermis sits atop the lower layer of the skin, the dermis, from which it is separated by a proteinaceous basement membrane⁴⁹. Microneedle arrays we designed and fabricated in this thesis have 600-700 μm height, which would only penetrate through the outer layer of skin into the epidermis layer without interfering with the nerve endings, enabling minimally invasive injection and extraction of interstitial fluid from the skin.

Interstitial fluid (ISF), or tissue fluid located in the epidermis, is a liquid surrounding the tissue cells of multicellular animals. Approximately 45 to 75% of the total body weight is composed of water, in which extracellular fluid (ECF) denotes all body fluid outside the cells. ISF is the main component of ECF, which constitutes the internal environment of the body that bathes all cells in the body. The extracellular fluid provides the medium for exchanging substances between the ECF and the cells, and this can occur through dissolving, mixing and transporting in the fluid medium⁵⁰. ISF has been proven to be a carrier of several of the most essential biomarkers in the body, and can also be considered as an alternative source of biomarkers compared to blood plasma. There is convincing untapped potential for diagnostics, such as allergy testing, drug discovery, and biomedical research.

In 2018, new organ termed as 'interstitium' was discovered in the body system after it was previously missed by scientists despite being one of the largest organs in the human body. The newly found organ, beneath the top layer of the skin, is also in the tissue layers lining the gut, lungs, blood vessels, and muscles⁵¹. The interstitium has a highly permeable blind-ended network of lymphatic capillaries, which is mainly responsible for collecting excess interstitial fluid. It transports lymph or chyle through a one-way low-pressure drainage system of interweaving collection vessels and incorporates

lymph nodes to large lymphatic trunks that drain into lymphatic ducts, which communicate with venous circulation⁵². This provides a bright foreground for the microneedle owing to its wide application in ISF research. Figure 1.8 shows a schematic summary of the histological findings.

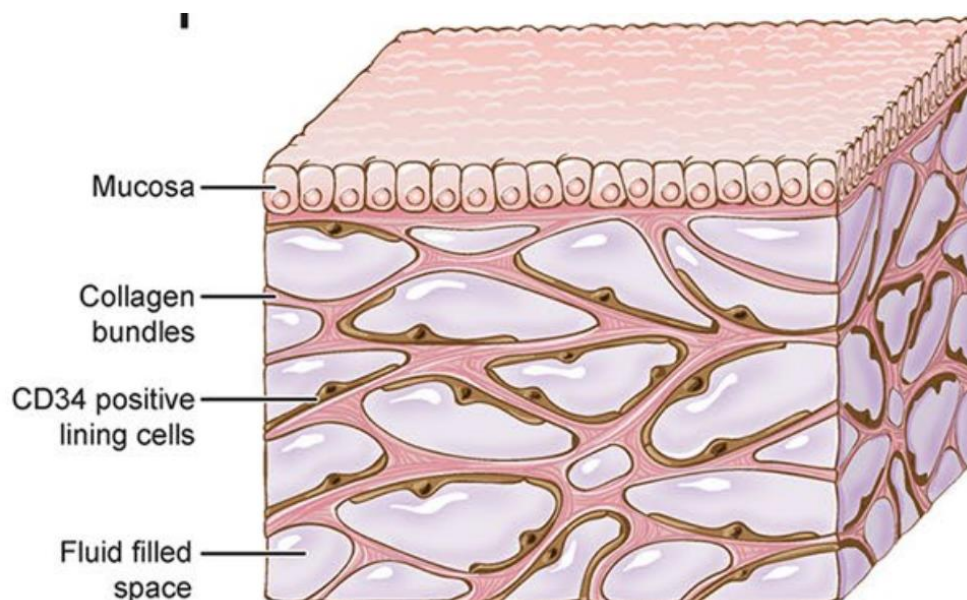


Figure 1.8 Schematic of the fluid-filled space supported by a network of collagen bundles lined on one side with cells⁵¹.

1.3 Classification of microneedles

1.3.1 In-plane microneedles and out-of-plane microneedles

Microneedles can be divided into two models based on the relationship between the direction of the needle tip and the substrate: in-plane microneedles and out-of-plane microneedles. The orientations of the two types of microneedles are different. For the out-of-plane microneedle, the tip is perpendicular to the substrate plane whereas the tip

of the in-plane microneedle is parallel to the substrate plane. For an out-of-plane microneedle, the height can't exceed the thickness of the wafer, limiting the penetration depth. However, it is possible to fabricate a 2D array of microneedles. On the contrary, in-plane microneedles can be very long but only 1D arrays can be fabricated.

Figure 1.9(a) shows a typical out-of-plane microneedle array, showing 350 μm high silicon microneedles on an SOI wafer. Figure 1.9(b) shows a typical in-plane microneedle array with a length of 1.2 mm.

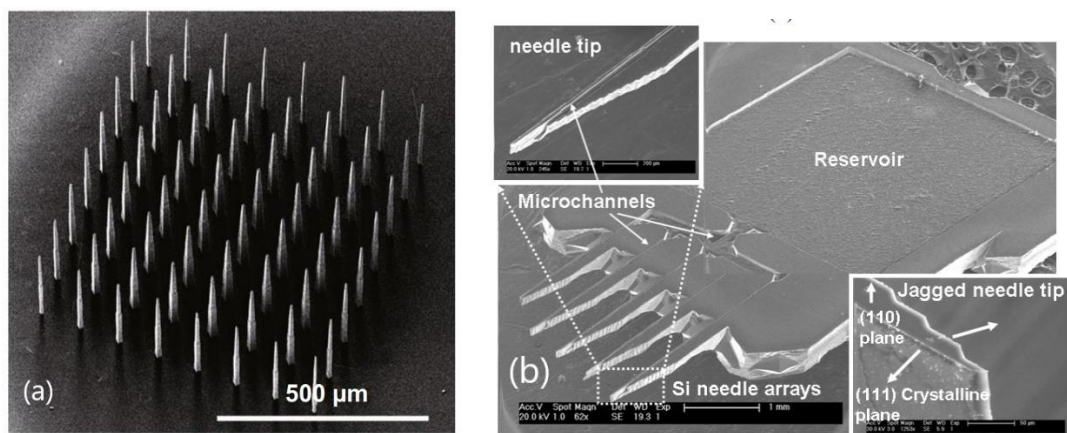


Figure 1.9 Out-of-plane and in-plane microneedles (a) 350 μm high, sharpened 2D silicon microneedle array⁵³; (b) 1.2 mm long silicon in-plane microneedles with microchannels⁵⁴.

1.3.2 Solid microneedles and hollow microneedles.

Initially, microneedles are formed in the solid state due to their convenience for fabrication compared to hollow microneedles¹⁸. Figure 1.10 (a) shows the first out-of-plane solid microneedles for transdermal drug delivery applications^{55,56}. As for the hollow microneedles, the first hollow out-of-plane microneedles were produced by McAllister et al. in 1999⁵⁶. Figure 1.10 (b) shows the 150 μm long hollow silicon microneedles fabricated by combining the fabrication process of solid silicon microneedles with deep reactive ion etching (Bosch process) to form a needle bore^{56,5657}.

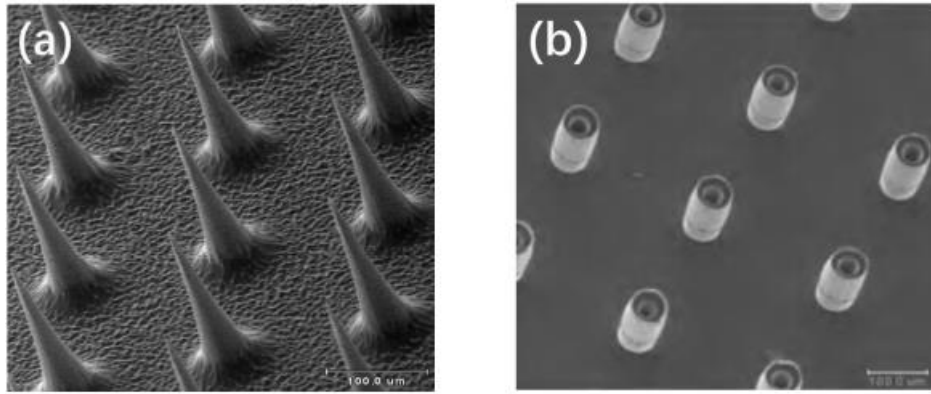


Figure 1.10 (a) Solid silicon microneedles used for transdermal drug delivery. Approximately 80 μm at the base and 150 μm long solid microneedles were fabricated in silicon using DRIE, and featured sharp tips with a tip radius below 1 μm ⁵⁵. (b) The first hollow out-of-plane microneedles by McAllister et al. The silicon needles are 150 μm long and were fabricated through DRIE using Bosch process⁵⁷.

In 2000, Stoeber and Liepmann created a novel type of hollow silicon microneedles^{56,58}. The needle bores are produced from double-sided processing consisting of a backside DRIE process and a frontside isotropic dry etching to form the needle shape. The process flow of the flat-tip microneedle fabrication is presented in Figure 1.11, and Figure 1.12 shows hollow silicon microneedle arrays with (a) pointed tips and (b) flat tips. The needles were approximately 200 μm in height with a lumen diameter of 40 μm .

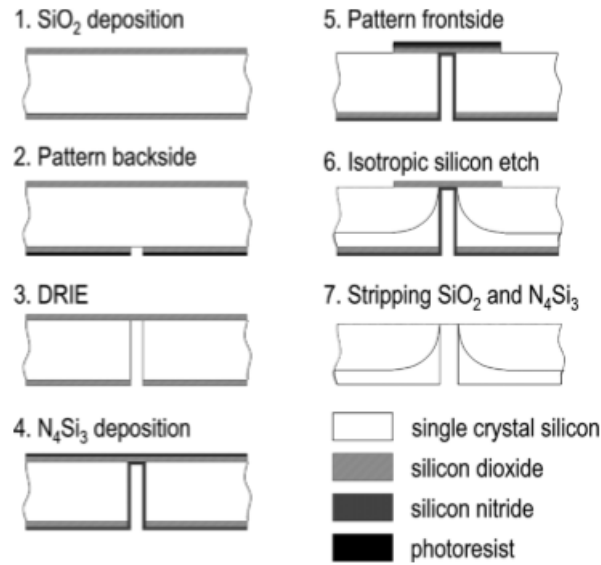


Figure 1.11 Schematic of process flow for the fabrication of silicon out-of-plane microneedles⁵⁸.

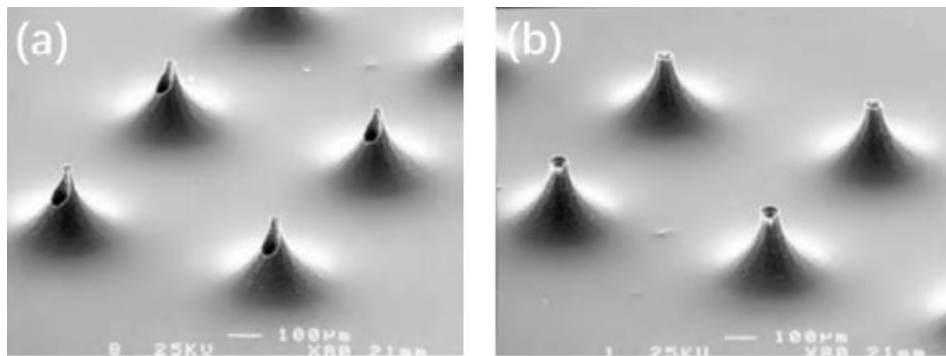


Figure 1.12 Hollow silicon microneedles by Stoeber and Liepmann⁵⁸. The 200 μm long needles are fabricated by Bosch DRIE and sharpened by isotropic dry etching. (a) Pointed tip; (b) Flat tip.

Clogging is a major concern when testing microneedles on humans for drug delivery or biofluid extraction; therefore, it must be considered cautiously. In 2003, Griss and Stemme developed and demonstrated the concept of side-opened microneedles that achieved a relatively low fluidic resistance. A three-dimensional needle structure was proposed, in which the needle bores were located at the shaft of the needle as shown in Figure 1.13⁵⁹.

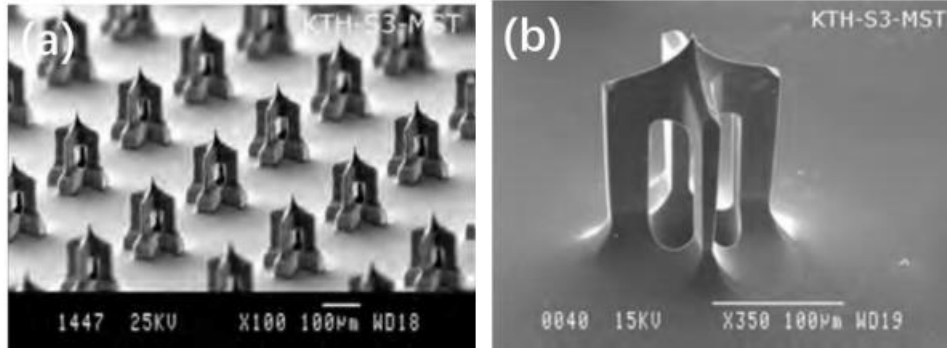


Figure 1.13 210 μm high, cross-shaped, hollow, side-opened, silicon microneedles fabricated by Griss and Stemme. (a) Needles with a 50 μm long base shaft. (b) Needles without a base shaft⁵⁹.

This side-opened design was accepted by the academia and further developed by Roxhed et al. in 2005⁶⁰. The process flow is illustrated in Figure 1.14. Compared to the previous design, the aspect ratio was increased in the new design by producing the silicon needles significantly longer to 400 μm as shown in Figure 1.15. Meanwhile, the geometry of the tips changed from cross-shaped to circular to form a sharp and well-defined tip. Thus, the new design exhibited superior penetration characteristics. In terms of all reported tests with this design, needles penetrate skin using thumb force without any other external help⁵⁶.

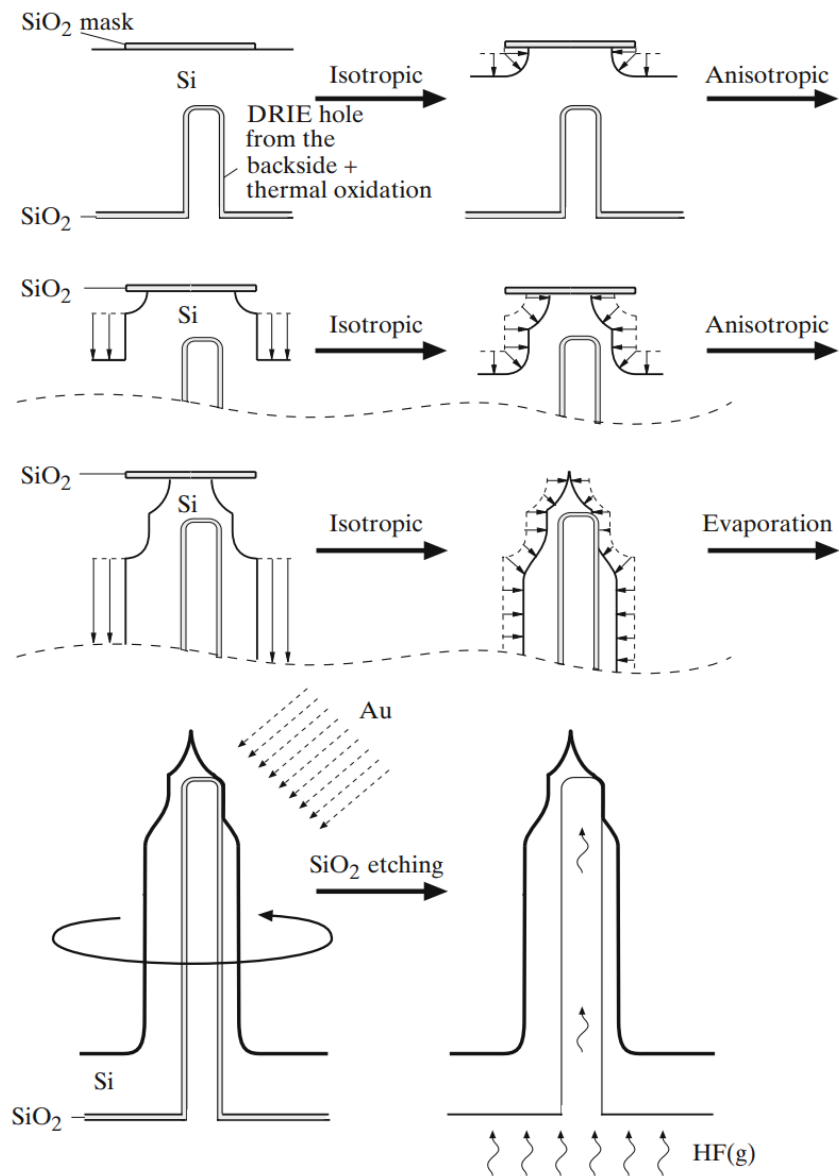


Figure 1.14 Process flow for the fabrication of circular side-opened hollow microneedles⁶¹.

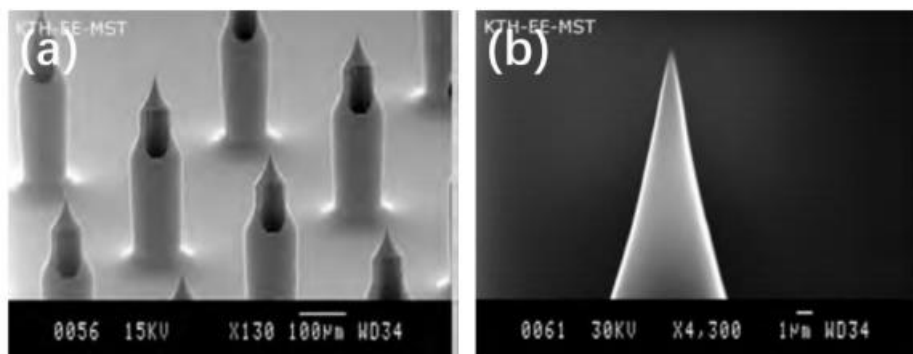


Figure 1.15 The circular side-opened design developed by Roxhed et al. (a) 400 μm long, ultra-sharp, side-opened microneedles. (b) Magnified view of the microneedle tip. The tip-radius is below 100 nm⁶⁰.

In 2003, a wet etching approach using potassium hydroxide was introduced in the fabrication process of silicon microneedles to sharpen the tips of the needles, resulting in intersecting crystal planes. Gardeniere et al. presented tetrahedrally shaped hollow silicon microneedles by combining DRIE and KOH etching techniques together⁶². Figure 1.16 shows the fabrication process for the microneedles. Frontside patterning and etching were first processed, followed by backside hole etching to etch through the wafer. Next, a silicon nitride protection layer was deposited to cover the entire sample and the front-side silicon nitride was removed by plasma etching. Anisotropic etching via KOH etching was then performed to form a slope with a sharpened tip. Finally, the remaining silicon nitride was removed to complete the fabrication process. Figure 1.17 (a) shows a typical result of a 350 μm high microneedle with a triangular tip shape; the base is 250 μm , the maximum hole has a width of 70 μm , and Figure 1.17 (b) presents a microneedle design with a rounded tip. Additionally, this new alternative method to fabricating sharp-tip microneedles was being commercialized by NanoPass Ltd.. This company also collaborated with GlaxoSmithKline in microneedle-based vaccine delivery and joint patents⁶³.

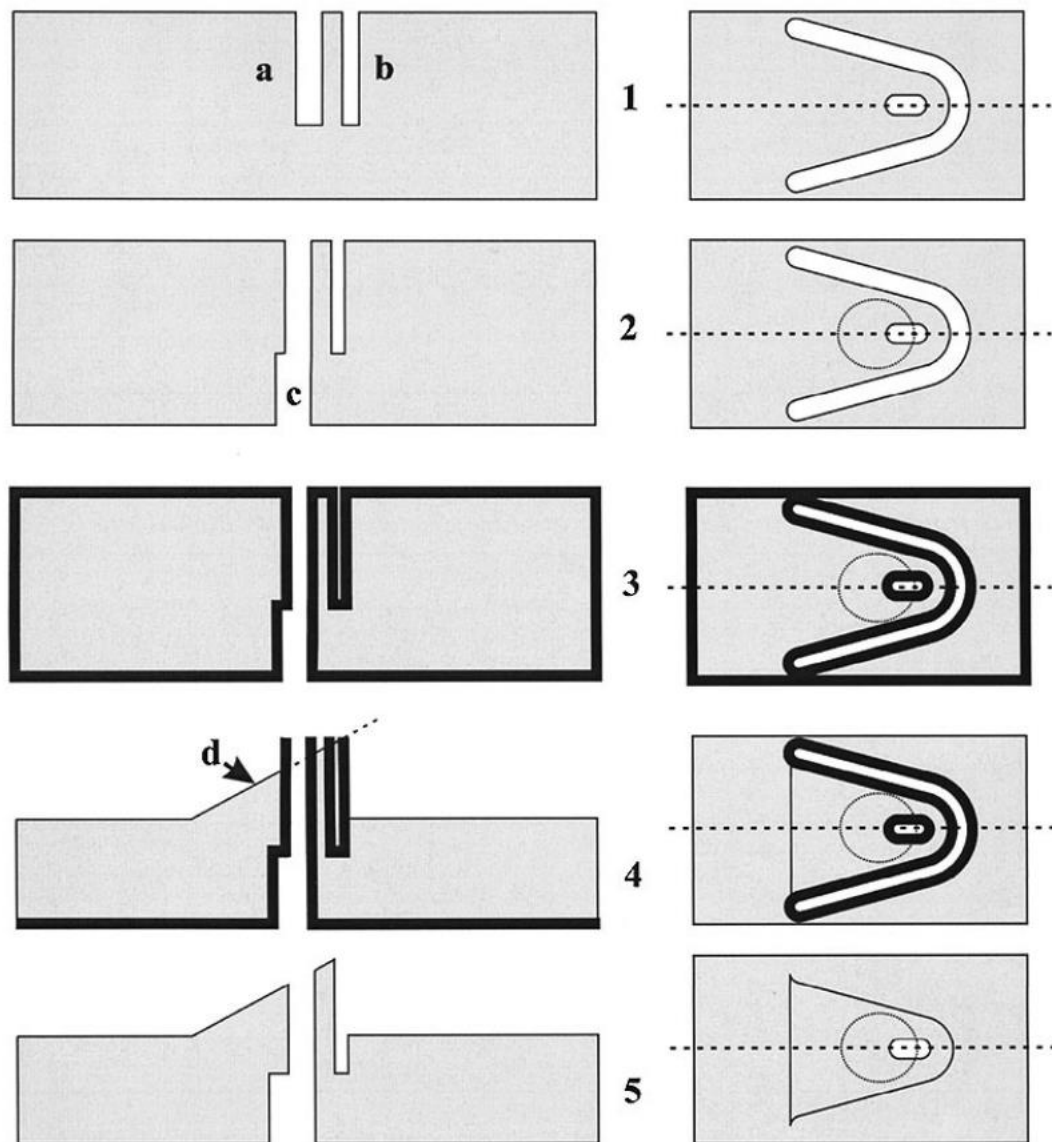


Figure 1.16 Fabrication process for microneedle using DRIE and KOH wet etching. Left, cross-sectional drawing of the sample at dotted line; Right, top view of the process⁶².

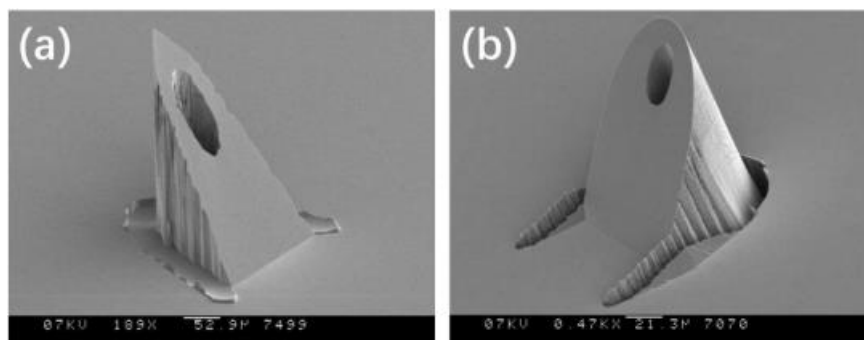


Figure 1.17 (a) SEM micrograph of a 350 μm high microneedle, with a base of 250 μm .
(b) SEM picture of a microneedle with a tip having large radius of curvature⁶².

In 2023, one fabrication process for hollow microneedles using combined KOH wet etching and DRIE dry etching was proposed by O'Mahony et al.⁶⁴. As shown in Figure 1.18, first, PECVD oxide was deposited on the backside of a 1-mm thick double side polished wafer. Then, LPCVD oxide and nitride were deposited. After frontside nitride and oxide patterning, KOH wet etching was performed to form cone-shaped silicon needles. Later, aluminum was covered on the surface of the microneedles as the protection layer. Backside hole etching was performed afterwards to complete silicon microneedle fabrication process. Figure 1.19 shows the SEM image of the microneedles with 500 μm height.

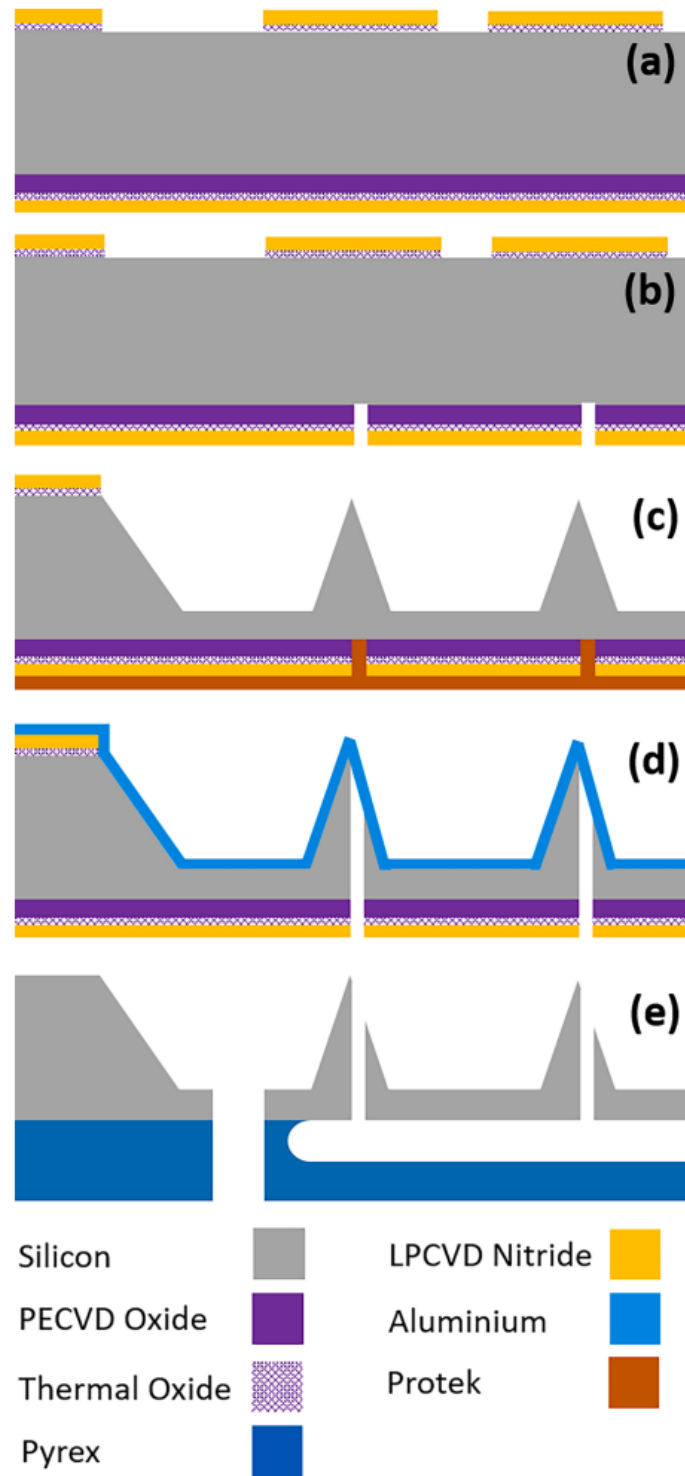


Figure 1.18 Fabrication process for microneedles using the combination of KOH wet etching and Bosch process⁶⁴.

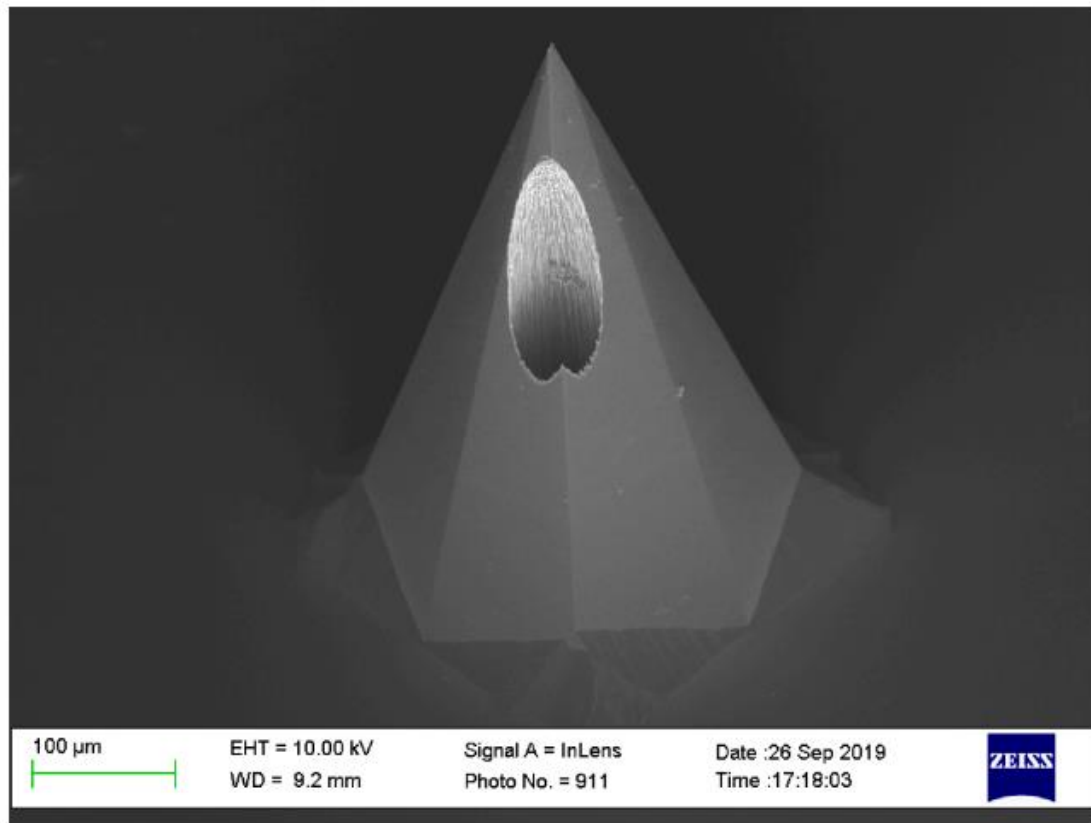


Figure 1.19 SEM image of a 500 μm tall microneedles with a 50- μm diameter offset pore⁶⁴.

Over the years, the position of the hole relative to the needle body for the hollow microneedle has also changed. Initially, the hole was formed right on the center of the top of the needles. The “volcano shape” needles (Figure 1.12(b)) have a concerning drawback that the tip is not sharp enough to penetrate the skin since the contact area surrounding the hole is still too large. To increase the pressure, an offset of the hole (Figure 1.12(a)) was introduced to make the tip sharper. To make the tip even sharper, researchers have attempted to open the hole on the sidewall of the needle (Figure 1.15). However, the process flow is extremely complex. Later, with the introduction of wet etching based on KOH, researchers could form a beveled sharp tip with a hole on the top of the slope using a relatively simple method (Figure 1.17).

1.3.3 Different materials of microneedles

Since the microneedles are likely to be used in medical devices, for material selection, it is necessary to consider the biocompatibility, safety, and stability of the material. Silicon was the first material to fabricate microneedles owing to its good biocompatibility, mechanical strength, and thermal and chemical stability. Ceramics are a great choice due to their extraordinary mechanical properties, while metals such as titanium, stainless steel, and aluminum are also sometimes desired. Polymers are another popular choice since polymers have advantages such as low cost, easy formability, and short processing cycle. Moreover, the invention of dissolving microneedles based on polymers has broadened the application of microneedles. Figure 1.20 shows some examples of microneedles in different materials.

In this thesis, we mainly focus on the fabrication process of silicon out-of-plane microneedles.

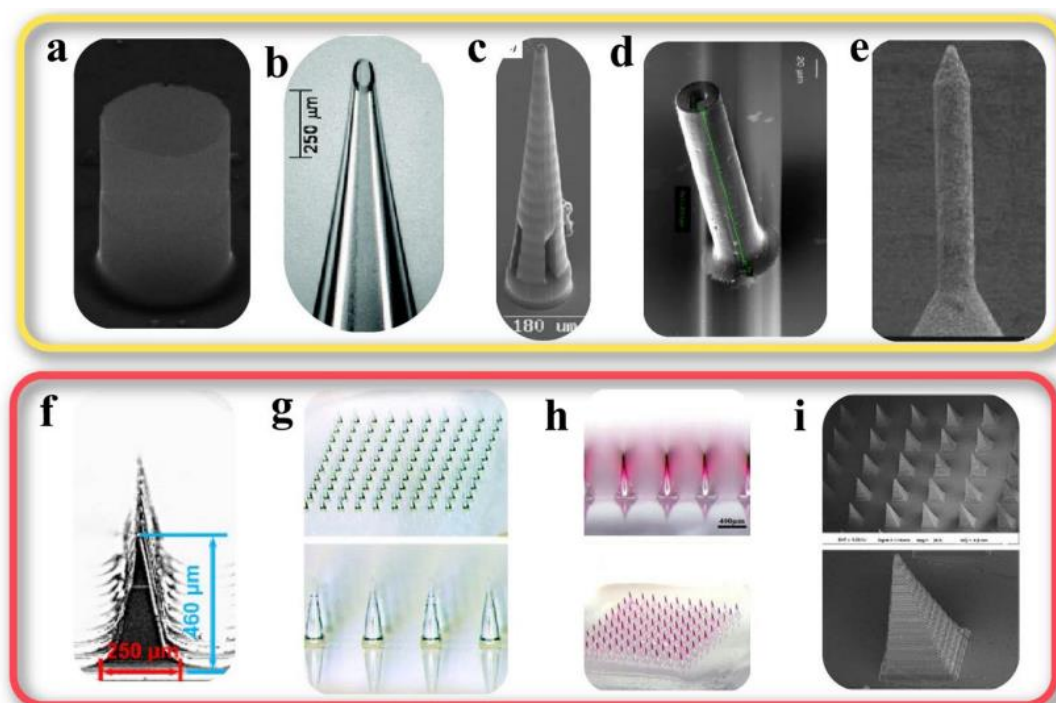


Figure 1.20 Examples of microneedles in different materials³². (a) Silicon⁶⁵; (b) Glass⁶⁶; (c) Ormocer⁶⁷; (d) Glassy carbon⁶⁸; (e) Steel⁶⁹; (f) Polyvinylpyrrolidone⁷⁰; (g) Polylactide⁷¹; (h) Polyvinylalcohol⁷²; (i) Polypropylene⁷³.

1.4 Critical parameters of microneedles

Several key parameters are essential for evaluating the performance of silicon out-of-plane hollow microneedles. When designing the microneedle, these parameters should be considered. First is the height of the microneedle. The height refers to the vertical distance between the needle's base and the needle's tip. The height can't be too short because the needle should be long enough to penetrate the epidermis. The mean thickness of the epidermis on the arm, which is usually adapted for injection, is approximately $100\text{ }\mu\text{m}$ ⁷⁴. In this way, the height should be at least $150\text{ }\mu\text{m}$. Also, the needle can't be too long. If the needle is too long, the needle will reach pain receptors in the dermis, causing a lot of pain. In summary, typically, the height of the microneedle ranges from 300 to $1500\text{ }\mu\text{m}$, and $600\text{ }\mu\text{m}$ is considered as an optimized height.

Another parameter is the aspect ratio. For microneedles, aspect ratio is defined as the height divided by the widest part of the needle. Microneedles with a higher aspect ratio are more slender, causing less damage to the skin but increasing the risk of fracture. Conversely, microneedles with a lower aspect ratio are broader, potentially causing more skin damage and increasing penetration difficulty.

Microneedle density is also important on a microneedle chip. Excessively dense arrangement of microneedles necessitates greater force for skin penetration, increasing the risk of chip fracture. Conversely, insufficient microneedle density requires a larger area for drug injection or interstitial fluid extraction, thereby reducing efficiency.

Chapter 2

Specific microfabrication techniques for microneedle fabrication

This chapter introduces critical microfabrication techniques integral to microneedle fabrication: thin-film deposition, photolithography, wet etching, and dry etching.

2.1 Thin film deposition

Film deposition is typically the first step in the microfabrication process. Silicon nitride is an excellent material for surface passivation. A variety of methods can be used to achieve specific applications⁷⁵. Thin-film deposition can be divided into chemical vapor deposition (CVD) and physical vapor deposition (PVD). CVD involves low pressure chemical vapor deposition (LPCVD), plasma enhanced chemical vapor deposition (PECVD), and atomic layer deposition (ALD), while PVD consists of thermal/e-beam evaporation and sputtering. Each technique has its own strengths, depending on the deposited materials, target thickness, and desired properties of the thin film. Typically, chemical vapor deposition is used for the deposition of non-metallic material such as SiO_2 , SiN_x , while physical vapor deposition is usually used for the deposition of metals or metal oxides such as aluminum, chromium, copper and their oxides. Importantly, one material deposited using different techniques may exhibit different properties and qualities. Figure 2.1 shows the steps of thin-film growth in a chemical vapor deposition process. First, the substrate was exposed to volatile precursors from supplied gases. Subsequently, the reaction on the substrate surface produces the desired deposition. Normally CVD involves various physical and chemical processes involving complex fluid dynamics because gases flow into the reactor and participate in complex reactions, and by-products are transported out of the reactor.

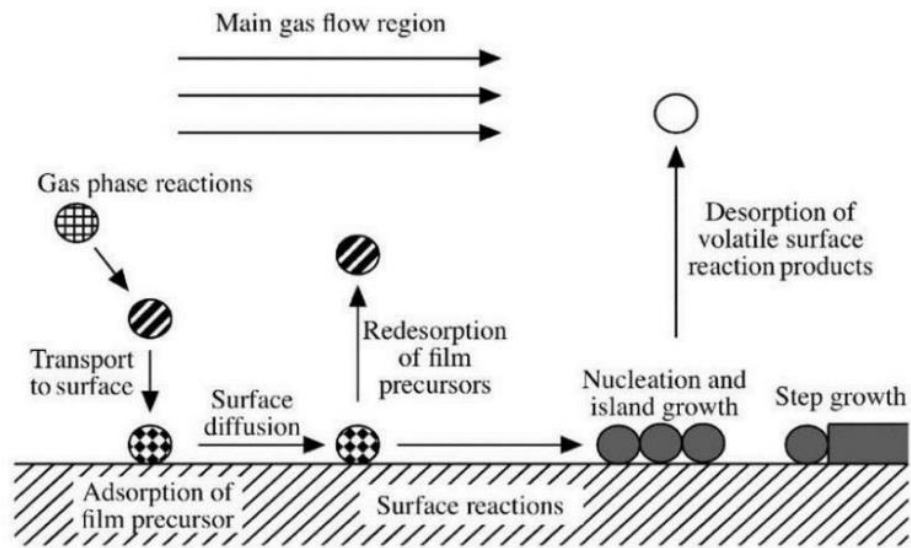


Figure 2.1 Overview of thin film growth on substrate surface in chemical vapor deposition⁷⁶.

In this thesis, SiN_x was deposited via PECVD. PECVD permits energetic reactions at low temperatures compared to LPCVD. Figure 2.2 shows a typical PECVD reactor.

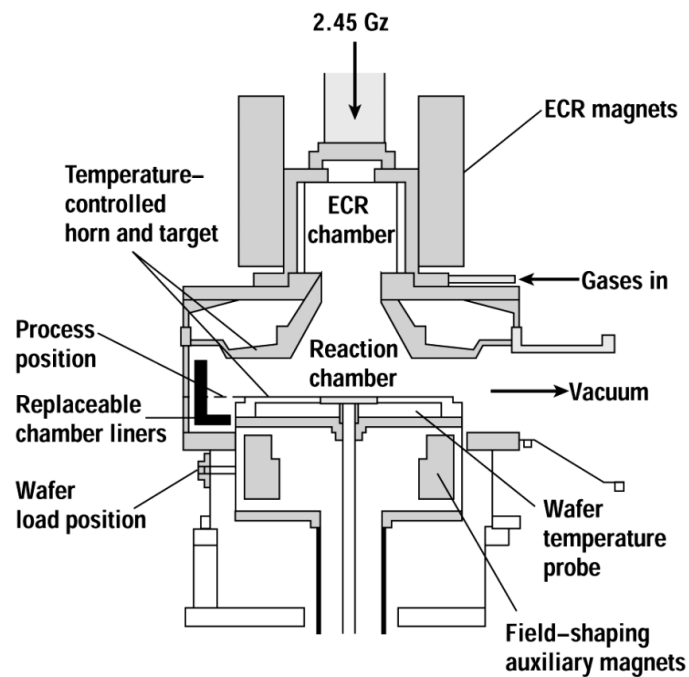


Figure 2.2 Diagram of PECVD reactor⁷⁷, here using a high density ECR (electron-cyclotron resonance) plasma source instead of the more popular parallel-plate plasma source.

2.2 Thermal oxidation

Thermal oxidation is an essential technique in microfabrication that can form high-quality silicon oxide, which can serve as a mask or insulating layer. The oxidation of silicon can be divided into four steps. First, oxygen is diffusively transported across the diffusion layer in the vapor phase adjacent to the silicon oxide-vapor interface. Oxygen is then incorporated at the outer surface into the silicon oxide film. Next, oxygen is diffusively transported across the silicon oxide film to its interface with the silicon lattice. Finally, oxygen reacts with silicon in the inner lattice. Tube furnaces are usually used for thermal oxidation, but muffle furnaces can also be utilized since air contains the oxygen required for thermal oxidation (Figure 2.3).



Figure 2.3 Nabertherm muffle furnace up to 1100 °C (Courtesy to Nabertherm).

2.3 Photolithography

Photolithography is a process that adopts high-intensity ultraviolet (UV) light and a photomask to prepare a polymer pattern on a silicon wafer^{78,79}. As a well-established method commonly applied in the semiconductor industry today, photolithography is the root technology of MEMS technology because it is the basis of the following complicated semiconductor processes for fabricating MEMS devices. Moreover, most current information technologies rely on microchips that are designed and fabricated by microfabrication techniques. It facilitates circuit integration through patterning and etching of multiple device layers and creating vias and interconnects with modest alignment tolerances⁸⁰. Figure 2.4 shows a photograph of SUSS MA6, a lithography system we used for alignment and UV exposure of resist-coated wafers.



Figure 2.4 MA/BA6 Mask and Bond Aligner (Courtesy to SUSS MicroTec).

The basic photolithography process is employed to selectively remove some parts of a thin film (or the bulk of a substrate) by changing the chemical structure/solubility of the photoresist consisting of a light-sensitive compound and a mixture of polymers. In this manner, the geometric pattern is successfully transferred from the photomask to the photoresist on the substrate. Photoresists can be classified into two types. For the positive resist, the illuminated area becomes highly soluble during development after exposure, whereas a negative photoresist is composed of monomers or polymers that polymerize or crosslink to form insoluble polymers under specific wavelengths of ultraviolet (UV) exposure. As a result, various required structures can be defined perfectly and efficiently by coating different types of photoresists.

Another method to complete photolithography is maskless lithography. Unlike the traditional photolithography process, this state-of-the-art technique can complete

photolithography via a CAD file (usually in GDS format) without the need for a photomask. The pattern is exposed directly onto the substrate surface using a spatial light modulator (SLM), which serves essentially as a programmable mask. The system takes the design file and simply “writes” the pattern to the resist-covered substrate. This direct-write process could skip the entire time-consuming and expensive photomask process; it is favorable to redesign the pattern multiple times and expose it immediately⁸¹. The typical equipment was manufactured by Heidelberg Instruments. Figure 2.5 (a) shows the Heidelberg DWL 66+ equipment we used, and Figure 2.5 (b) illustrates the SLM principle.

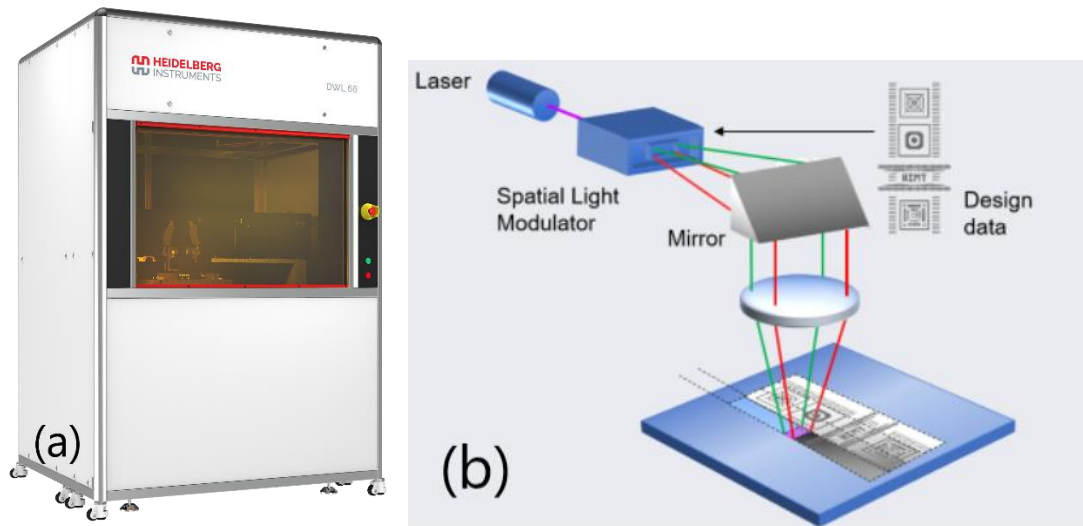


Figure 2.5 (a) Heidelberg DWL 66+ laser lithography system⁸². (b) The principle of SLM in Heidelberg Direct Write Lithography system⁸¹.

As shown in Figure 2.6, the photolithography process usually starts with deposition (e.g., spin-coating) photoresist onto a substrate, followed by soft baking in order to evaporate the solvent. A photomask with the desired structural feature is well positioned above the substrate using a mask aligner, and then UV light travels through and focuses on the photoresist layer that is soluble or insoluble depending on which type of photoresist is spun onto the substrate. Diverse exposure modes can be determined based on the position of the substrate, and the contact condition between the photomask and

substrate can be soft contact, hard contact, proximity, or projection mode. For a positive resist, the area covered by metal (usually chromium) of the mask stays insoluble; on the contrary, the exposed area will be dissolved during subsequent development, leaving behind a patterned layer of photoresist. This defined pattern acts as a barrier to protect the underlying film from wet or dry etching in the subsequent process. Finally, the pattern is successfully transferred from the photomask to the substrate.

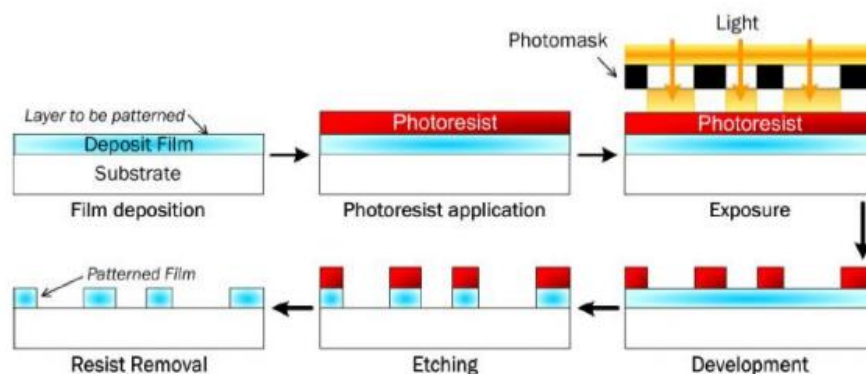


Figure 2.6 Basic photolithography process using positive photoresist: the exposure and etching process that allows one to transfer a pattern to the film/wafer⁸⁰.

In summary, conventional photolithography can only achieve a resolution of approximately 1 μm , but advanced tools with many resolution enhancement techniques (RET) have been developed and applied over the years such as off-axis illumination (OAI), optical proximity correction (OPC), and phase shift masks (PSM), leading to a resolution of less than 10 nm. In this project, photolithography is a key step to transfer the pattern from photomasks and GDS II files that we designed to photoresist followed by wet or dry etching to define pillar and hole structures.

2.4 Etching

As a pattern-transfer method, etching is an essential process for selectively removing layers from the surface of a wafer to fabricate the desired patterns on the device. A

photoresist patterned using lithography can be utilized as a masking material to protect the substrate from etching. They are also frequently used in the microfabrication processes of semiconductor devices for wafer planarization, isolation and cleaning.

There are several important metrics of the etching process, such as uniformity, etch rate, selectivity, anisotropy, and undercut. The etch rate is defined as the etched length in a specific direction per unit time. Normally, the etch rate is influenced by the etchant concentration, temperature, and pressure. Figure 2.7 shows silicon etch rates depend dramatically on KOH concentration and etch temperatures. Selectivity is defined as the ratio of the etch rates of different materials. To define a high aspect ratio structure, such as deep holes and high pillars, the masking material is supposed to have high selectivity to protect the underlying film. Figure 2.8 illustrates the poor selectivity resulting in defects during the etching process. Anisotropy or isotropy is another critical parameter often discussed in the etching process. Figure 2.9 shows the difference between isotropic (uniformly in all directions) and anisotropic etching (etch only occurs in the vertical direction).

	Temperature(°C)						
%KOH	20	30	60	70	80	90	100
10	1.49	3.2	25.2	46	82	140	233
15	1.56	3.4	26.5	49	86	147	245
20	1.57	3.4	26.7	49	86	148	246
25	1.53	3.3	25.9	47	84	144	239
30	1.44	3.1	24.4	45	79	135	225
35	1.32	2.9	22.3	41	72	124	206
40	1.17	2.5	19.9	36	64	110	184
45	1.01	2.2	17.1	31	55	95	158
50	0.84	1.8	14.2	26	46	79	131
55	0.66	1.4	11.2	21	36	62	104
60	0.5	1.1	8.4	15	27	47	78

Figure 2.7 Silicon etch rates in ($\mu\text{m}/\text{h}$) for various KOH concentrations and etch temperatures⁸³.

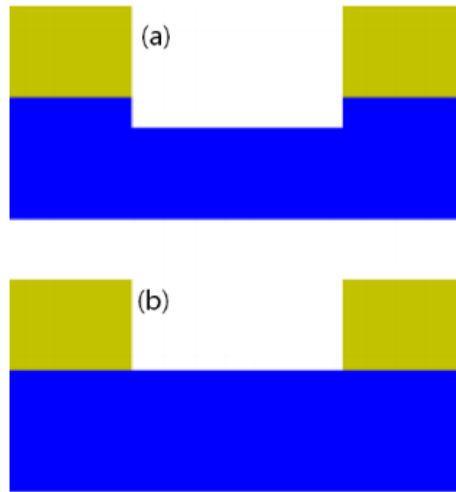


Figure 2.8 A graphical representation of (a) a poor selectivity that causes the etchant to attack the bottom layer material while removing the top layer, (b) a high selectivity that results in etching out the top layer without affecting the underlying layer⁸⁴.

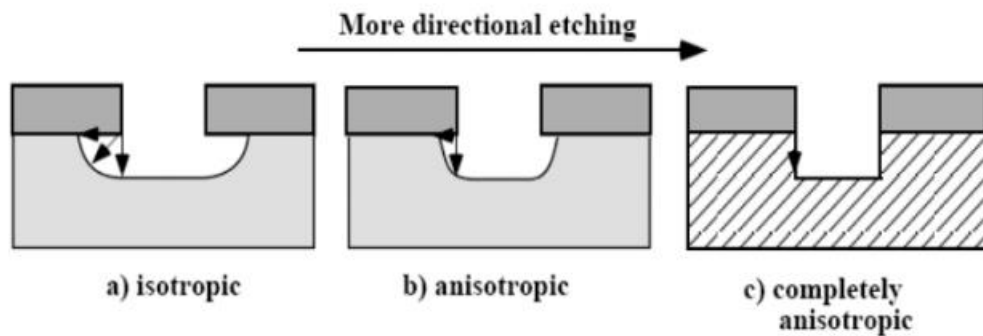


Figure 2.9 A schematic of (a) isotropic etching of silicon (b) partially anisotropic (c) completely anisotropic⁸⁵

Etching can be classified into two main categories based on the type of etchant used: wet etching (liquid-based etchants) and dry etching (plasma-based etchants). Wet etching is easily implemented by immersing the wafers in a chemical solution with a quick reaction, however, it is difficult to control and define precise feature sizes that are smaller than 1 μm . In addition, the production of chemical wastes is a concern. On the other side, for dry etching, also called plasma etching, reactive ions in the gas phase are formed in a vacuum system to sputter or vaporize the materials, which is much easier to control than wet etching. Furthermore, dry etching is able to obtain <100 nm feature

size. In our microneedle fabrication process, both dry etch and wet etch are performed in the experiments.

2.4.1 Wet etching

As mentioned above, wet etching is the etching of solid materials into liquid or gaseous compounds in a chemical solution. This is completed by dipping or spraying chemical solution onto the substrate. Wet etching can efficiently fabricate silicon, oxide, and metals into a relatively large feature size with some dimensional loss. Usually, several chemical reactions happening in a single wet etching process that consumes the original reactants and produces new species.

Figure 2.10 shows three key steps in the wet etching process: (1) diffusion of the chemical etchant, (2) chemical reactions occurring at the surface, and (3) removal of the byproducts via diffusion. For wet etching, it is important to achieve good etching uniformity and a consistent etch rate, so that nowadays spray etching is progressively applied in industry rather than immersion etching.

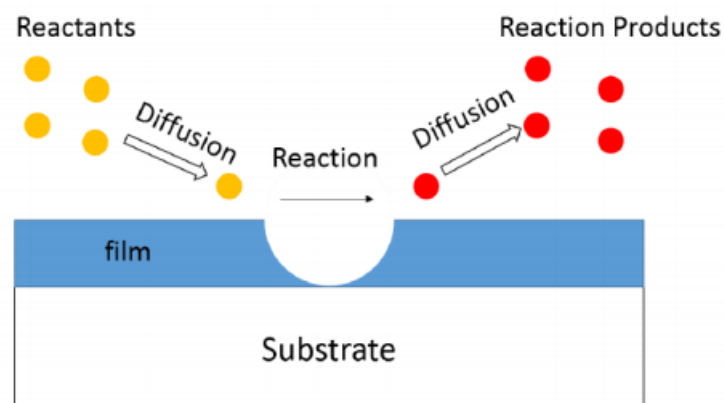


Figure 2.10 A schematic of wet etching process: (1) the diffusion of the reactants to the reacting surfaces, (2) the chemical reaction at the surface, (3) the transportation of the products away from the surface via liquid flow⁸⁶.

Both anisotropic and isotropic etching can be achieved using wet etching. For anisotropic etchants of silicon, the common choice is alkaline liquid solvents, such as potassium hydroxide (KOH), ethylenediamine pyrocatechol (EDP), and tetramethylammonium hydroxide (TMAH). Alkaline solvents can perform anisotropic etching of bulk silicon because the etch rate varies dramatically on different silicon crystalline planes. Figure 2.11 shows the three major planes in cubic unit silicon termed as (111), (100), and (110) by Miller index. As the density of the Si atoms, (111) plane is larger than the other two planes; as a result, a slower etch rate is expected on the (111) plane⁸⁷.

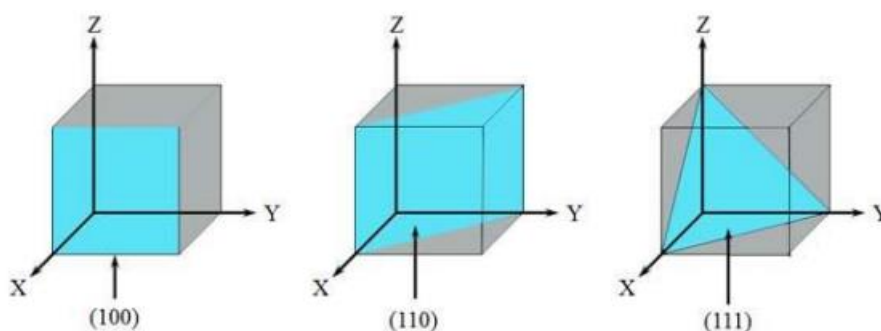


Figure 2.11 A graphical representation of silicon crystal planes⁸⁷.

Figure 2.12 shows the profile of the silicon bulk with different orientation after KOH anisotropic etching. Because the (111) plane has the slowest etch rate, it is exposed after KOH etching; consequently, for the (100) wafer, 54.7° slope is formed, and for the (110) wafer, trenches with vertical sidewalls are fabricated.

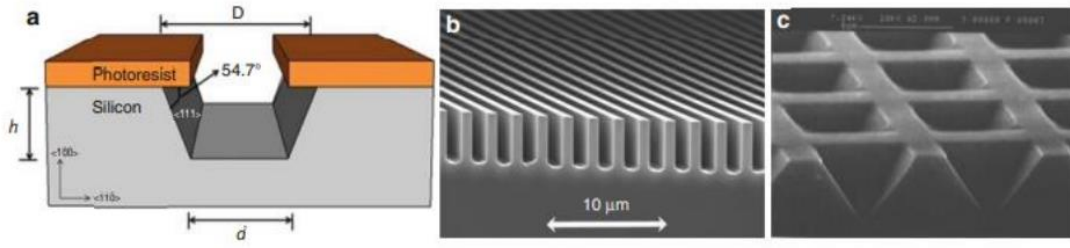
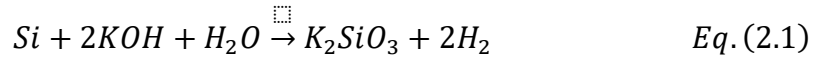
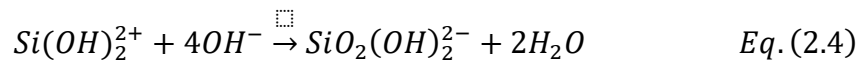
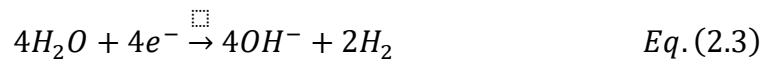
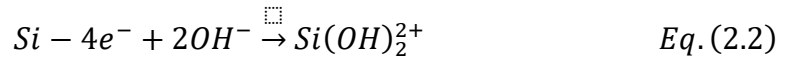


Figure 2.12 Silicon bulk profile after KOH etching⁸⁸. (a) Schematic diagram of cross-section of (100) oriented silicon etched by KOH solution. (b) SEM image of KOH etched (110) oriented silicon with line pattern. (c) SEM image of KOH etched (100) oriented silicon with square pattern.

To explain the reaction mechanism of alkaline wet etching, we used KOH as an example. Generally, the overall chemical equation is Eq (2.1).



This equation can be divided into three sub-reactions: one oxidation reaction (Eq. (2.2)), one reduction reaction (Eq. (2.3)), and one following reaction to form a water-soluble complex (Eq. (2.4))



Several factors influence the etch rate of KOH etching. As shown in Figure 2.13, the etch rate increases exponentially with increasing temperature, according to the Arrhenius equation.

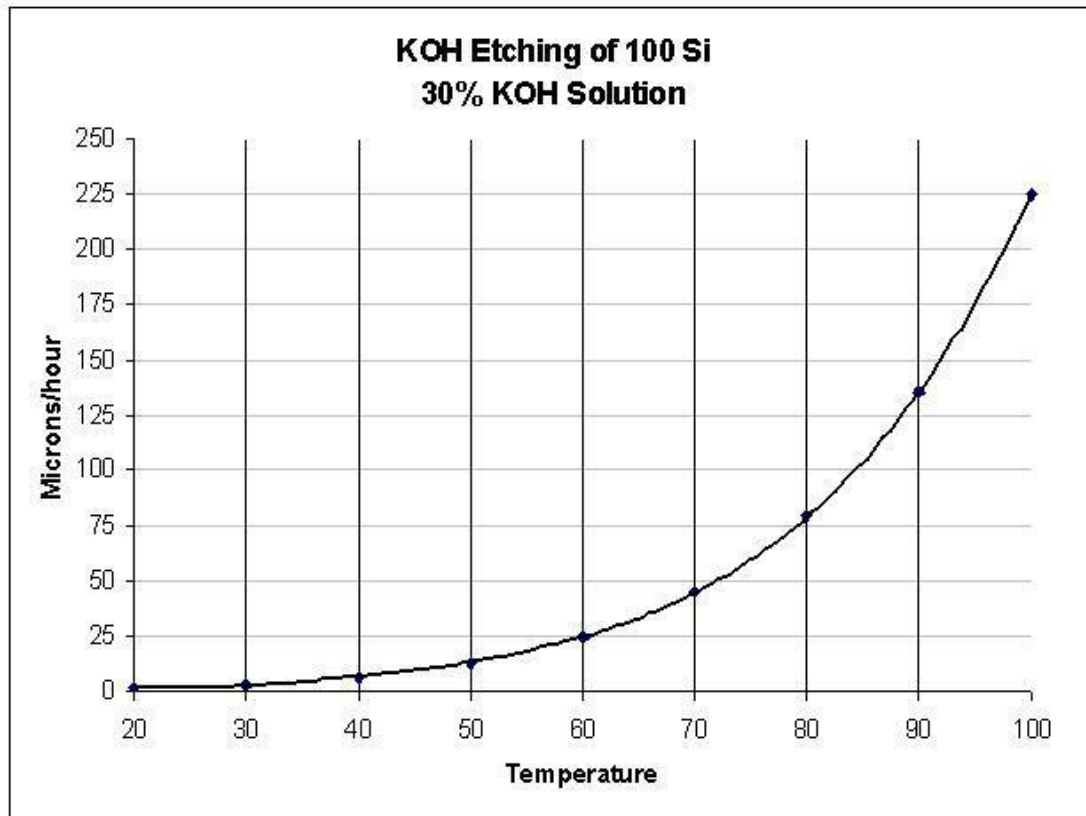


Figure 2.13 (100) Si etch rate vs. the temperature for 30% KOH solution⁸⁹.

However, for the relationship between the etch rate and KOH concentration, as shown in Figure 2.14, as the concentration increased, the Si etch rate initially increased but then decreased, which is counterintuitive. This is because water not only acts as a solvent, but also participates in the reaction, and an increase in the concentration of KOH means a decrease in the concentration of water.

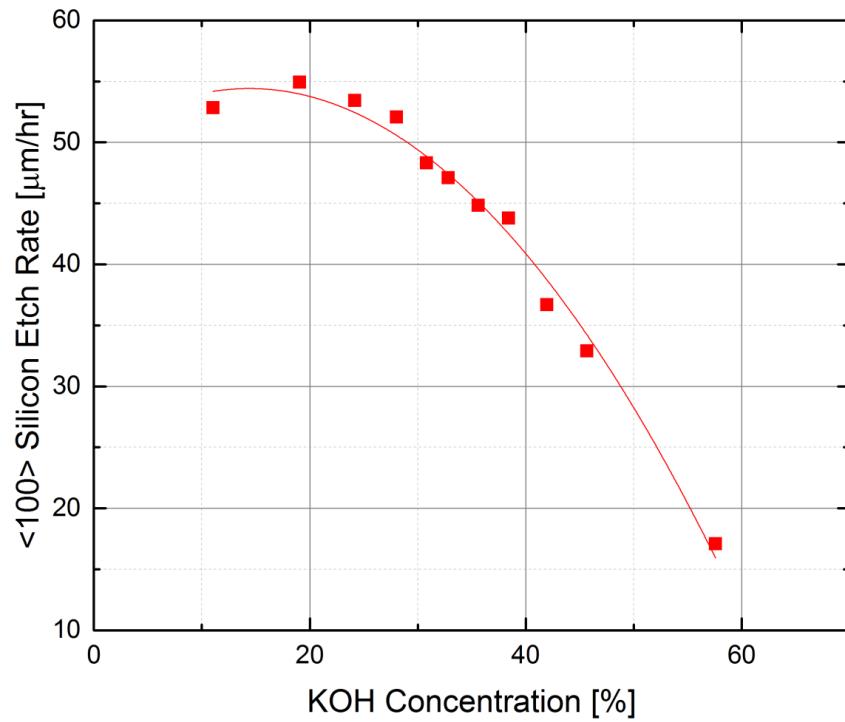


Figure 2.14 Etch rate of the (100) silicon crystal plane as a function of KOH concentration at 72 °C⁹⁰.

Silicon nitride (SiN) is the perfect choice for selecting an etching mask for alkaline etching. The etch rate of SiN is extremely low. The selectivity between LPCVD SiN and Si is 30000, and 7000 for PECVD SiN. As for the SiO₂, the etch rate for SiO₂ in TMAH is ~0.2 nm/min at 80 °C (Figure 2.15(a)), while in KOH, it is 5 nm/min at 80 °C (Figure 2.15(b)). Therefore, for TMAH etching, silicon oxide is also a good choice for etching masks. However, for KOH etching, silicon oxide is not as effective as a mask.

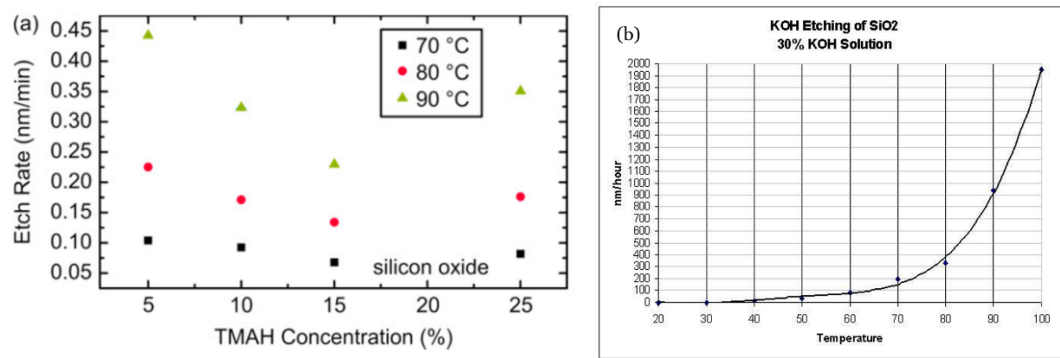


Figure 2.15 Etch rates of silicon oxide in (a) TMAH⁹¹ and (b) KOH⁸⁹.

Additionally, surfactants such as isopropyl alcohol (IPA), cationic ammonium salt of poly (ethylene glycol) (ASPEG), and Triton X-100 containing 100% iso-octylphenoxy polyethoxyethanol can be added to the solution to alter the etching behavior^{92,93,94,95}. For KOH etching, IPA can be added to change the etching profile of silicon. Without surfactants, as shown in Figure 2.16, the (110) plane has a higher etch rate than the (110) plane. In contrast, after IPA was added to saturation, the etch rate of the (110) plane was lower than that of (100). During the etching process, the (110) planes can develop in the sidewalls when the edges of the etching mask are aligned in the (110) direction and the etch rate ratio $R(100) / R(110)$ is higher than 1. As a result, adding IPA fulfills this requirement. The molecules of the compounds are supposed to preferentially adsorb on the (110) surface, hindering access to the reactants and, thus, slowing down the etching process⁹⁶ (Figure 2.17). For TMAH etching, Triton X-100 is a good choice as a surfactant, which is characterized as one of the best additives in TMAH to expose the (110) plane and obtain minimum undercutting^{97,98}.

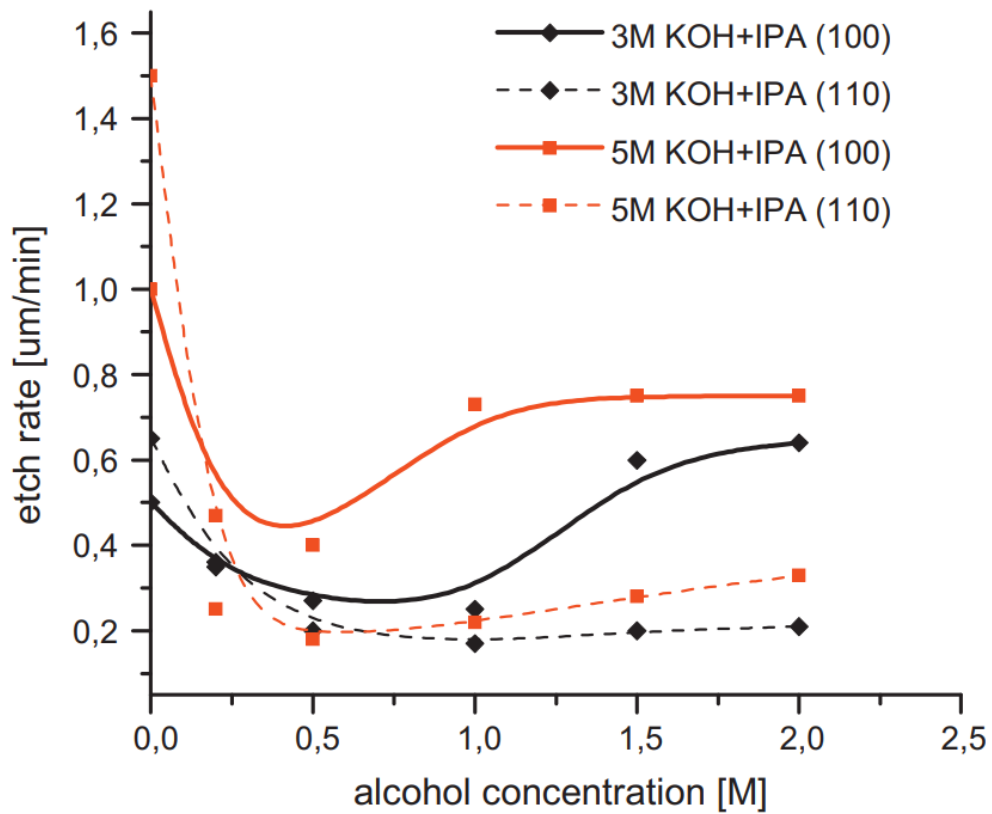


Figure 2.16 Etch rates of (100) and (110) Si surfaces in 3M and 5M KOH solution vs. alcohol concentrations⁹⁹.

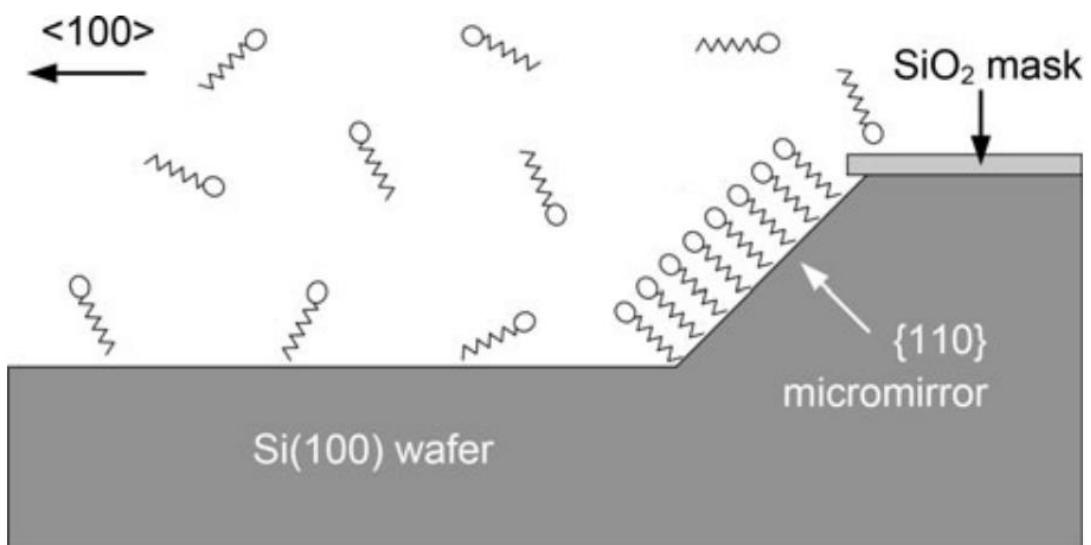


Figure 2.17 Schematic illustration of adsorption of surface active compound molecules like IPA and Triton X-100 on the (110) surface during silicon anisotropic etching in alkaline solution. The molecules adsorb with their hydrocarbon chains⁹⁶.

Due to the anisotropy attained by KOH wet etching, silicon microneedle structures with high accuracy and reproducibility can be fabricated. Wilke et al. proposed a systematic method of microneedle manufacturing with well-defined structures in 2005¹⁰⁰. Figure 2.18 shows the process flow. A standard, p-type bare silicon wafer with (100) orientation was used. Next, wet etching of silicon microstructures with high index crystal planes forming microneedle shapes is performed using 29% KOH at 79 °C. After a certain etch depth, the (111) crystal planes are etched away by faster etching planes, forming an octagon at the base. The needle shape is defined by eight high-index crystal planes, here as (312) planes¹⁰⁰. Figure 2.19 presents the result of one single microneedle shape with a height of 280 μm .

In this fabrication process, the (111) sidewall plane dominates at the beginning since the corner formed by the (111) and (001) planes is concave whereas for the concave corner, the plane with the slowest etching rate appears. However, once etching starts, the side corner formed by two adjacent slopes (e.g., (111) plane and (1-11) plane) are a convex one; and for convex corner etching, the stabilized plane would be that having the fastest etching rate, here for this etchant composition/temperature and original mask layout, the fastest etching plane is thought to be (312).

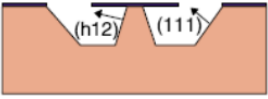
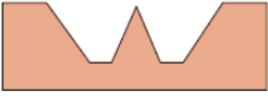
	Side View	Process step
1		LPCVD, 350Å pad oxide and 1000Å nitride double layer on silicon
2		Plasma etch to pattern mask
3		Wet etch using 29% KOH @ 79°C, etch of (111) crystal planes
4		High index crystal plane formation
5		Process stop

Figure 2.18 Wet etch process flow proposed by Wilke et al.¹⁰⁰

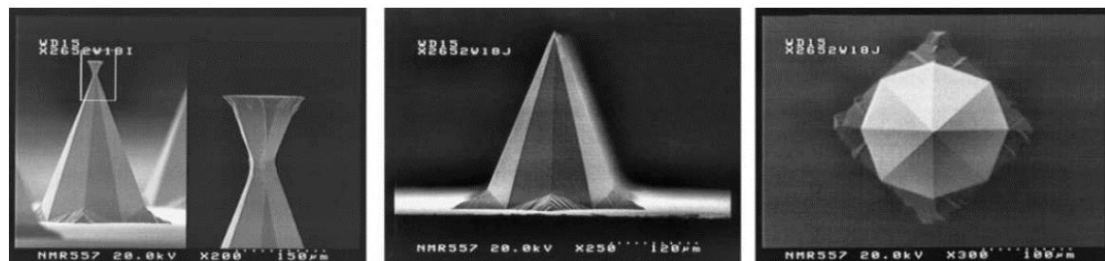
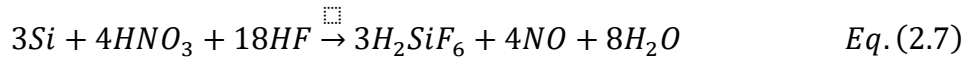
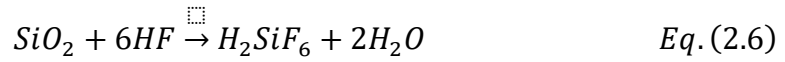
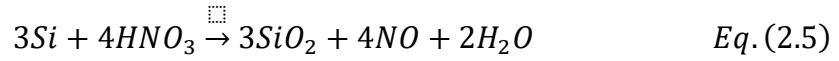


Figure 2.19 SEM micrographs of a single microneedle fabricated by Wilke et al.. Left, side view of the needle with a small negative top; middle, side view; right, top view¹⁰⁰.

Silicon etching using KOH or TMAH is anisotropic. As for the *isotropic* wet etching of silicon, HF-HNO₃ mixtures are widely used in today's semiconductor industry and in the production of solar cells. For example, HNA is an isotropic silicon etchant containing hydrofluoric acid, nitric acid and acetic acid (replaceable with water). HNA has a fast yet reproducible etch rate of silicon¹⁸. Figure 2.20 shows the etch rate of silicon. The solid curves correspond to the etching system in which acetic acid is the diluent, whereas the dashed curves correspond to the system in which water is the

diluent¹⁰¹. Robbins and Schwartz developed the etching mechanism. The reaction can be divided into two simultaneous steps: (a) HNO₃ oxidizes silicon to Silicon dioxide (SiO₂) (Eq. (2.5)), (b) HF etches SiO₂ and the gaseous product H₂SiF₆ was removed (Eq. (2.6)). Adding Eq. (2.5) and (2.6), the overall reaction is given by Eq. (2.7). In terms of chemical kinetics, for the case of low HF concentration, the key step is step (b), which means that the etch rate is limited by the oxide removal rate. HF diffusion to the silicon surface is the rate-limiting factor, which results in faster etching (shrinking/sharpening) of the pillar top, which receives more etchant via diffusion than the pillar base.



In terms of Bhandari's research on a wafer-scale microneedle etching technique in 2010, two-step etching containing one dynamic etching and one static etching was introduced¹⁰². Figure 2.21 illustrates the etching progression of this two-step etching process. Based on the theories above, a static wet etching system composed of the a mixture of HF (49%)–HNO₃ (69%) in a ratio of 1:19 by volume was set up to sharpen the silicon pillars into a sharp needle-shaped profile.

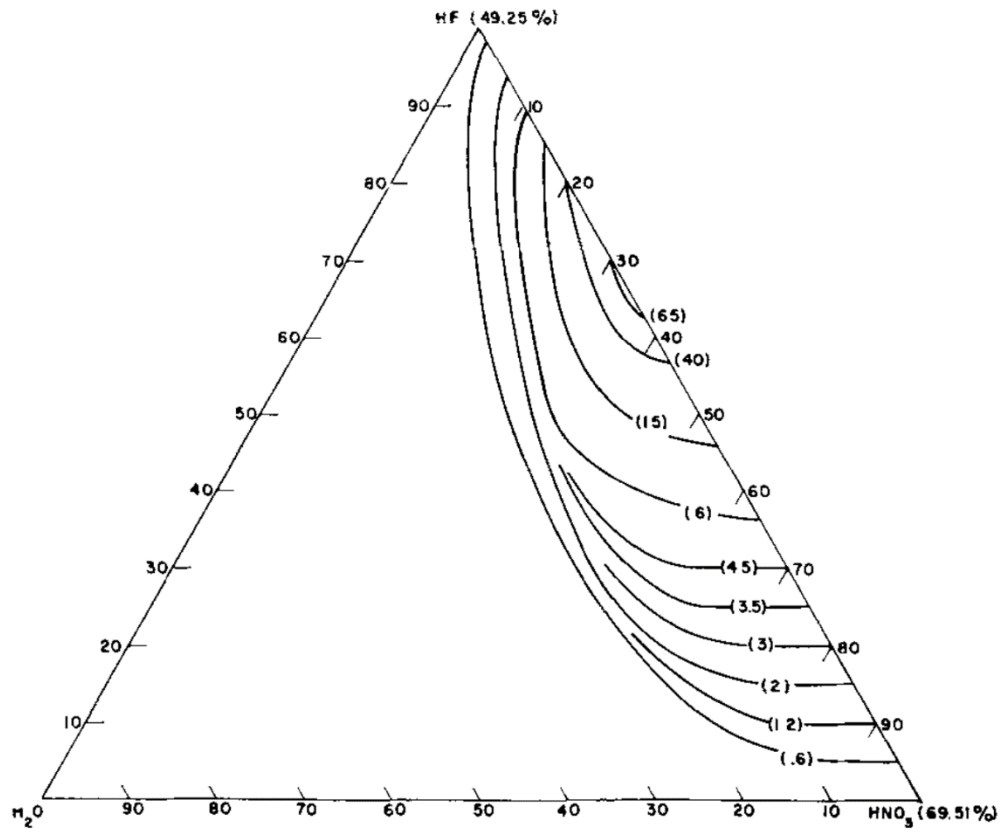


Figure 2.20 Curves of constant etch rate of silicon (mils/min) as a function of etchant composition in the system 49.25% HF, 69.51% HNO_3 , and diluent¹⁰¹.

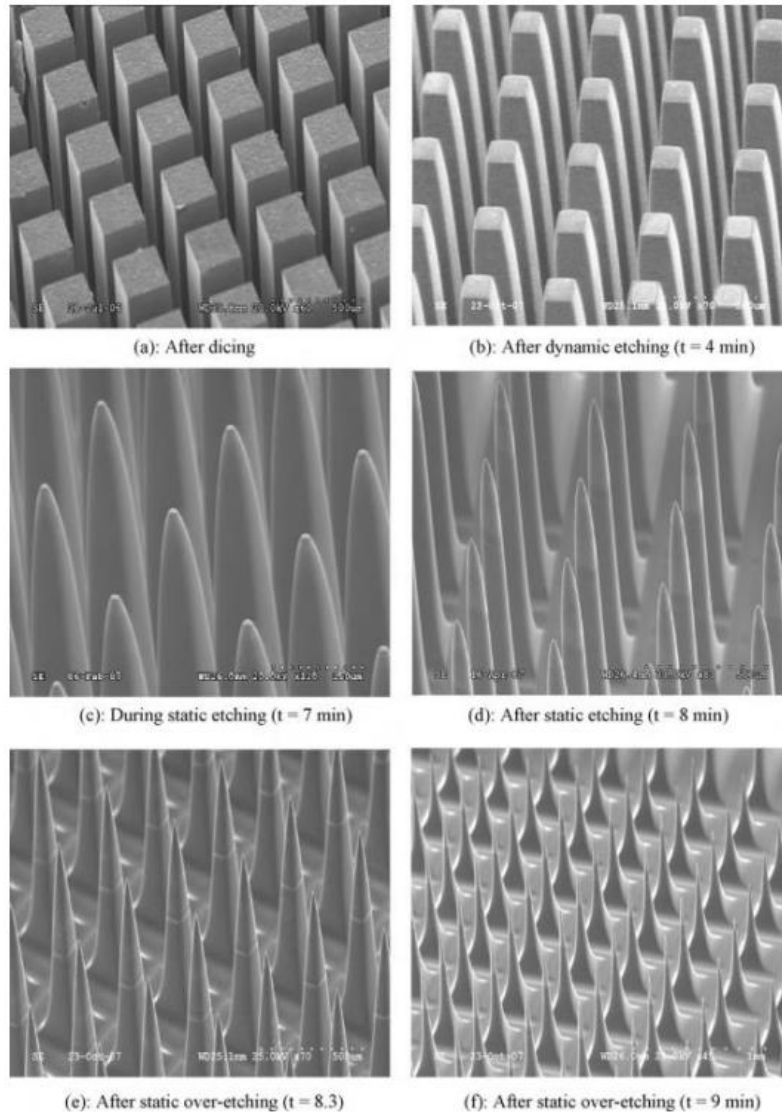


Figure 2.21 SEM images showing progress of needle formation from dicing through etching (a–f). The rectangular columns (a) are transformed into sharp needle shapes (d) during static etching (8 min). The high etch rate ($20 \mu\text{m}/\text{min}$) causes change in the geometry¹⁰².

2.4.2 Dry etching

Since its introduction in the 1970s, dry etching has been a vital process step that is widely used in microelectromechanical systems (MEMS) device fabrication. Compared

to wet etching, which is significantly affected by external factors such as temperature and humidity, dry etching is easy to control and capable of defining feature sizes that are smaller than 100 nm, and dry etching can easily attain anisotropic etching.

Plasma is the key factor in dry etching. It is formed by fully or partly ionized gas. The positive and negative charges are equal in plasma so that the plasma is electrically neutral. Electrons can be accelerated to form plasma in a high-energy state so that many processes that are not possible under normal conditions can take place.

Plasma etching involves three mechanisms: First, the material was removed by purely chemical reactions. Second, the material was removed by a combination of chemical reaction and physical bombardment. Third, the material was removed by purely physical bombardments. Correspondingly, the plasma etching can be classified into three categories: (1) chemical plasma etching (PE), (2) synergetic reactive ion etching (RIE), and (3) physical ion beam etching (IBE). Figure 2.22 shows these three mechanisms. PE produces isotropic profiles, high etch rates, and high selectivity, whereas IBE produces positively tapered profiles, low selectivity, and low etch rates. As a combined method, RIE combines the advantages of PE and IBE. RIE enables profile control due to the synergetic combination of physical sputtering with the chemical activity of reactive species with a high etch rate and high selectivity.¹⁰³

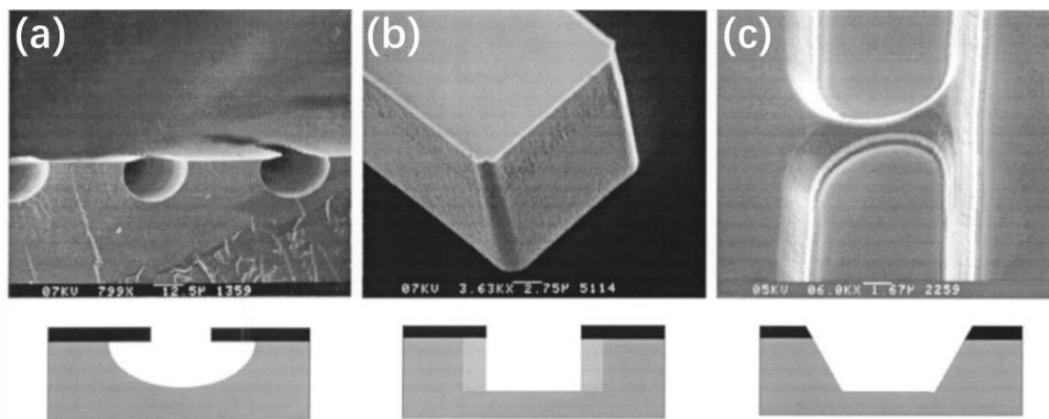


Figure 2.22 Typical etching profiles of the three basic mechanisms of dry plasma etching. (a) the chemical plasma etching (PE), (b) the synergetic reactive ion etching (RIE) and (c) the physical ion beam etching (IBE).

If etching relies only on ion bombardment or chemical reactions, it would be very ineffective and time consuming. Thus, reactive ion etching (RIE) has been considered a popular state-of-the-art etching technique combining physical process with chemical reactions to increase the etch rate. Technically, ion bombardment enhances the surface adsorption and byproduct removal to improve the reaction rate. Figure 2.23 shows different silicon etch rates for applying different gas phases with or without the aid of an Ar ion beam. We can see that the etch rate is extremely low when only physical bombardment or chemical reactions occur, however, we can achieve a high etch rate by applying ion-assisted chemical etching.

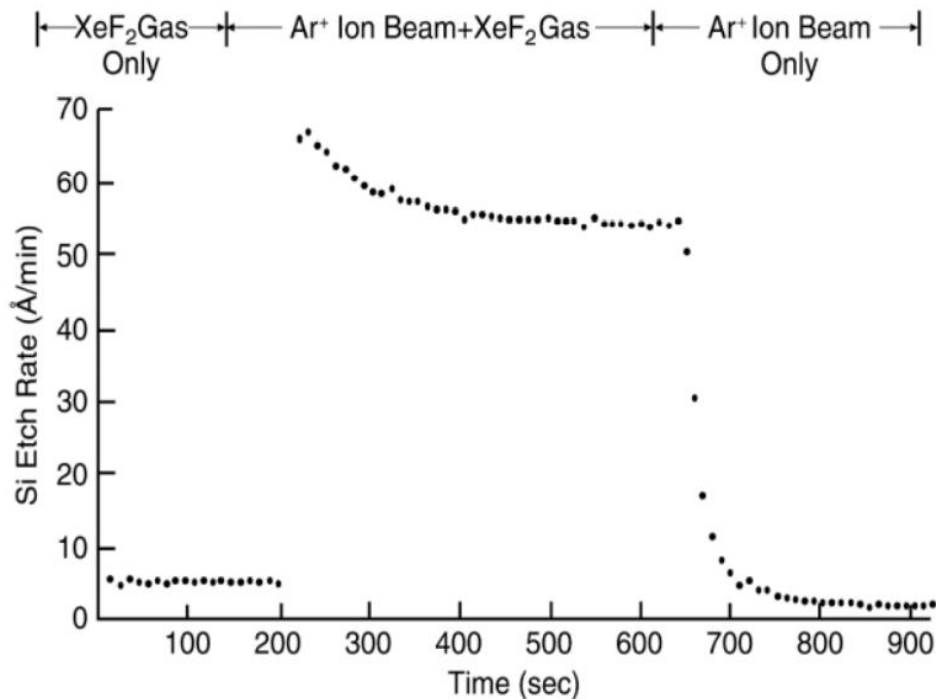


Figure 2.23 Etch rates of silicon as only XeF₂ gas (pure chemical etching, without plasma), only Argon ion beam (pure physical etching), and combination of them are introduced to the silicon surface. Ion-assisted chemical etch undoubtedly boosts the efficiency of the etching.

As shown in Figure 2.24, the RIE mechanism can be divided into four steps: First, a feed gas was introduced into the chamber, after which it was broken into free radicals, which are chemically reactive species. Then, diffusion through the boundary layer and along the surface of the wafer occurs. Once the reactive species reaches the surface, the

thermally activated reaction produces volatile species. Eventually, the etching product is desorbed from the wafer surface and vacuumed away through the gas stream.

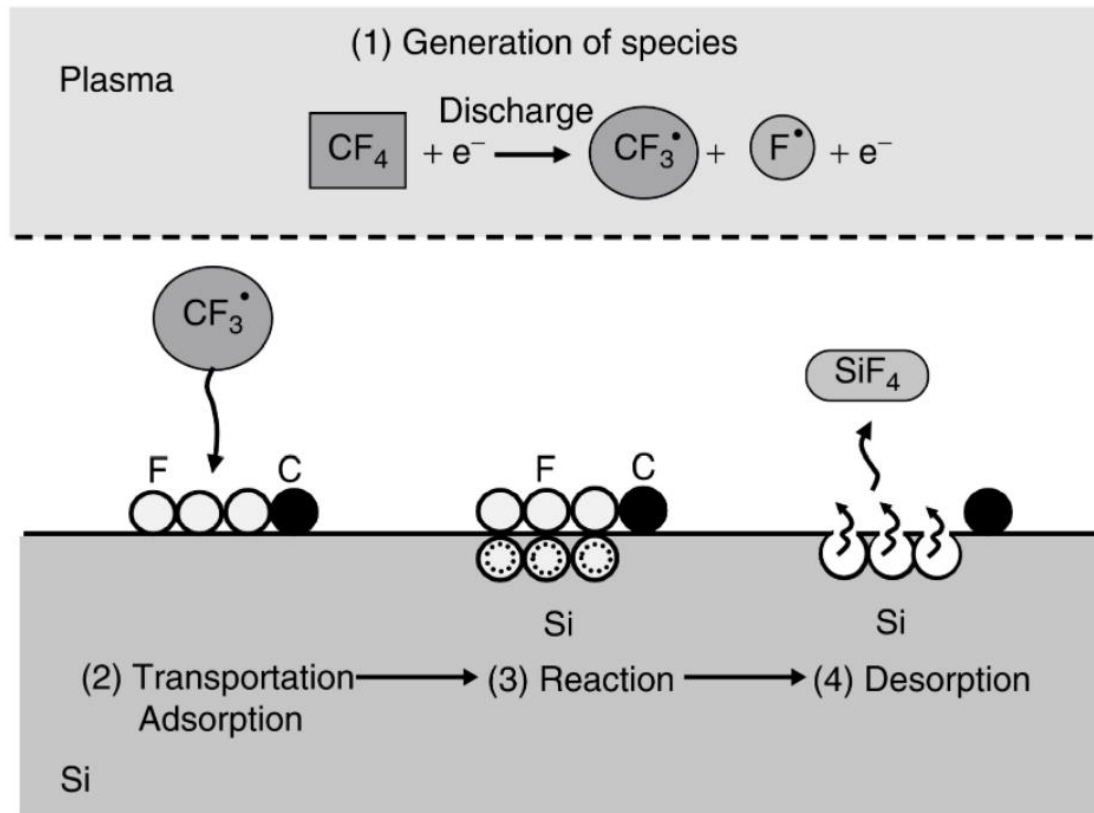


Figure 2.24 Reaction steps of RIE for the case of silicon etching.

Even if directional ion bombardments with low density are applied, isotropic etching is still unavoidable. Isotropic etching is a major problem when fabricating high-aspect-ratio microstructures. To obtain a high etch rate, high aspect ratio, and vertical sidewalls, deep reactive ion etching (DRIE) using the Bosch process has become an advanced technology for high-volume MEMS fabrication.

DRIE can achieve anisotropic etching of silicon. Moreover, DRIE could produce a high-aspect-ratio vertical profile with high selectivity without degrading the desired structures from etching in the lateral direction. For the Bosch process, there are two different plasmas (C_4F_8 and SF_6) performing sequentially in the chamber (referred as “cycles”). In one cycle, there were two switching steps within seconds. The details are shown in Figure 2.25. The first step was deposition (passivation). This step could

generate a passivating polymer film that prevents lateral etching of the exposed silicon sidewalls during the etching sub-cycles. The C_4F_8 molecule decomposes in the plasma and forms a Teflon-like chain polymer sticking to the exposed area. This Teflon-like polymer will not react with the SF_6 plasma, so that it can protect the covered area from further etching. Ion bombardment can physically and directionally sputter away the polymer on the horizontal surface, and the polymer on the sidewalls still exists to protect the profile. After deposition, an etch step was performed. SF_6 first reacts with silicon to produce gaseous SiF_4 which is pumped out of the system by the vacuum pump. Each etch step provides a short period (usually less than 10 seconds) of high etch rate isotropic silicon removal, which is normally less than one micrometer deep. By switching back and forth between the etching and deposition plasmas, the silicon was etched in an anisotropic fashion to the desired etch depth¹⁰⁴. In addition, the etch rate of the Bosch process depends on the percentage of exposed area of silicon on the wafer. Figure 2.26 shows the etch rate curve in terms of the standard Bosch process at University of Alberta. In this thesis, we mainly used four DRIE instruments to perform Bosch process. (1) Oxford PlasmaPro100 ICP-350 in Quantum NanoFab at University of Waterloo; (2) Oxford PlasmaPro100 Cobra in CIRFE Lab at University of Waterloo; (3) Oxford PlasmaPro100 ICP-350 at Zhejiang University, China; (4) Samco RIE-iPB800 in Tanwei Nanotechnology Co. Ltd.

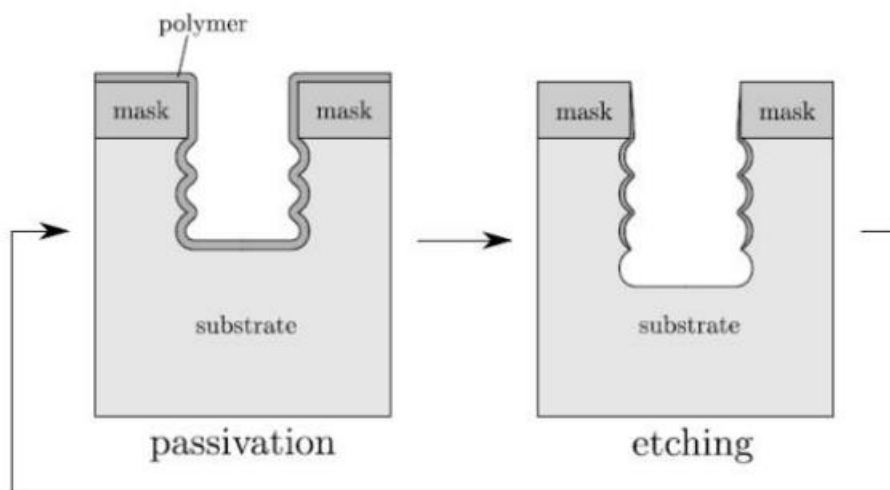


Figure 2.25 Bosch process and the alternation between the passivation and etching step.

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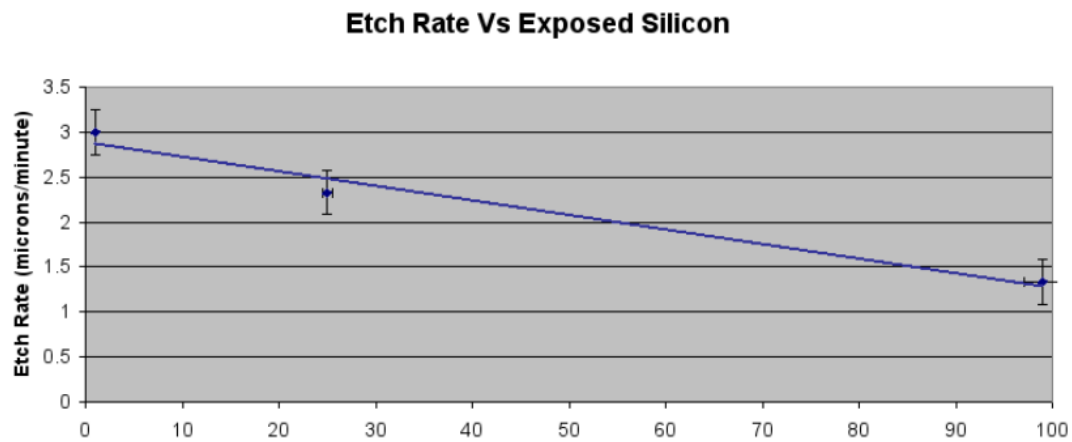


Figure 2.26 Etch rate curve related to the amount of exposed silicon.

In summary, wet etching can be easily implemented in the experiment with a quick reaction, however, it is difficult to control and define the precise feature sizes smaller than 1 μm . On the other side, although dry etching like DRIE process itself is an established methodology to create high aspect ratio structures such as high pillars and deep holes, developing an optimized recipe for the successful etching of hollow microneedles is a big challenge. In this thesis, both dry etching and wet etching were exploited in the experiments.

Chapter 3

Fabrication of silicon out-of-plane hollow microneedles by DRIE and HF-HNO₃ sharpening

This chapter delineates the design, comprehensive fabrication process, and resultant characteristics of silicon out-of-plane microneedles featuring sharp apices and off-axis pores. The fabrication methodology is predicated on DRIE for the etching of pillars and holes, and the subsequent sharpening of the pillars is achieved through a HF-HNO₃ treatment.

3.1 Overall design of silicon out-of-plane cone-shaped microneedles with sharp apex and off-axis pore

The process flow is illustrated in Figure 3.1. The entire process has three vital parts: backside hole etching, frontside pillar etching, and pillar sharpening. Starting from the double side polished wafer with thermal oxide, a double layer of AZ-P4620 photoresist (Merck, Germany) was spin-coated on the backside with a thickness of 17 μm , followed by standard photolithography. Next, Bosch process was performed on the backside of the wafer to etch holes with a depth of $\sim 300\text{ }\mu\text{m}$ and a diameter of 30 μm . Frontside photolithography was then implemented based on backside alignment, ensuring an offset of the hole structure in the pillar, which is exposed in wet etching sharpening. The offset of the hole is to make the needle tip sharper, otherwise it will form a “volcano shape” tip, reducing the sharpness. Another Bosch process was performed on the frontside to form the pillar arrays. For step (f), as detailed in Chapter 2, a static wet

etching system consisting of a solution of HF (49%) and HNO₃ (69%) mixed at a ratio of 1:19 by volume was set up in this work to sharpen the silicon pillars into a sharp needle-shaped profile. For the 200 μm high pillars etching, after 40-minute wet etching, we obtained highly uniform microneedle arrays with less than 5 μm diameter at the tip with an off-axis hole exposed. Figure 3.1(g) shows a 3D schematic of sharp microneedle array.

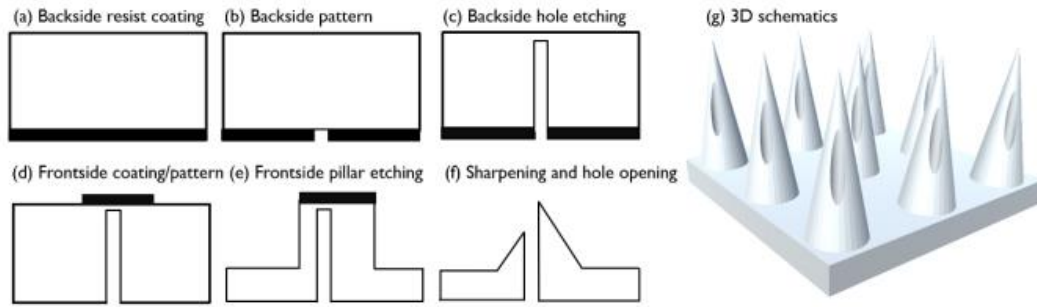


Figure 3.1 Schematic fabrication processing of hollow silicon microneedle arrays. (a) Backside resist coating; (b) Backside lithography; (c) DRIE on the backside for hole etching; (d) Lithography via backside alignment; (e) DRIE on the frontside for pillar etching; (f) Wet etch sharpening.

3.2 Backside hole etching

Cryogenic and Bosch-based DRIE can be considered as the two main technologies for high-rate DRIE, and the Bosch process is the only recognized production method since cryogenic DRIE usually needs to be treated below -100°C , and under such circumstances, photoresist or other masks often crack due to thermal-expansion mismatch. Moreover, the by-products tend to deposit on the nearest cold surface such as the substrate and electrode^{107,108}. For many applications of DRIE, the main goal is usually to produce trenches or other features of very high aspect ratio¹⁰⁹.

A major challenge in DRIE is aspect ratio dependent etching (ARDE). When the aspect

ratio of the structures increased, the etch rate decreased rapidly.^{110,111,112} In this case, the etch rate rapidly decreased with the aspect ratio of the etched structures. Above a certain critical point of the aspect ratio, the etch rate reaches an extremely low constant value¹¹³. The proposed mechanism is that the ion flux to the bottom of the structure decreases along with its aspect ratio, resulting in insufficient passivation layer removal¹¹². As such, holes with higher aspect ratios would start to pinch off at the bottom, and above a certain critical point of the aspect ratio, the etch rate would remain extremely low. Figure 3.2 (a) shows an example of the ARDE of trenches of varying widths. Figure 3.2 (b) illustrates the ARDE lag measured as trench depths normalized to that of a 100- μm -wide trench¹¹⁰. When we etched holes on DRIE in CIRFE lab (Oxford PlasmaPro Cobra 100), we also observed ARDE; Figure 3.2 (c) shows the change in the etch rate of holes as the aspect ratio. As shown in Figure 3.2 (c), when the aspect ratio reached 6, the etch rate was less than 1/3 of that in the open area (AR=0).

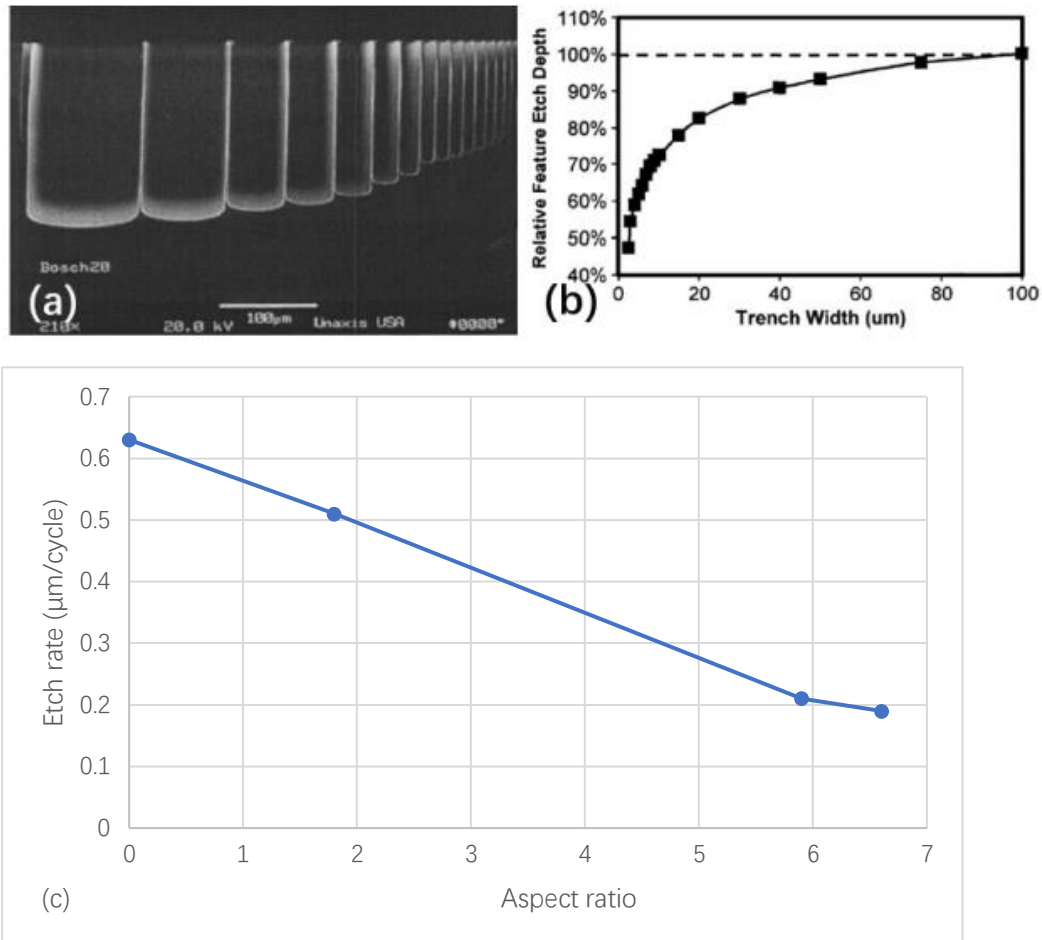


Figure 3.2 (a) ARDE lag exhibited in typical plasma etch process. The final etch depths

in wider trenches are larger. (b) A plot of trench depth normalized to that of a 100- μm -wide trench. An $\sim 50\%$ ARDE lag is observed in a 2.5- μm -wide trench¹¹⁰. (c) A plot of the connection between etch rate and aspect ratio according to the tests in Oxford PlasmaPro Cobra 100 in CIRFE Lab. A 70% decrease in the etch rate was observed when the aspect ratio was changed from 0 to 6.

Initially, we used the typical dual-phase standard Bosch process on the RIE in Quantum NanoFab consisting of a passivation step and an etching step. It was observed that this process suffers from ARDE when etching high aspect ratio holes. Consequently, we proposed a triple-phase “modified Bosch” process that has the distinctive feature of adding a depassivation step between the two steps of the standard Bosch, as shown in Table 3.1. The depassivation step utilizes energetic Ar ions to efficiently remove the fluorocarbon passivating polymers. This DRIE process provides highly directional (almost completely anisotropic) etching of holes of 200 μm in depth and 30 μm in diameter.

Table 3.1 Parameters of DRIE etching process with an RF frequency of 13.56 MHz.

Recipe	Standard Bosch at 15°C		Modified Bosch at 5°C		
Step	Passivation	Etching	Passivation	Depassivation	Etching
Gas	C ₄ F ₈	SF ₆	C ₄ F ₈	SF ₆ /Ar	SF ₆
Flow Rate	160 sccm	160 sccm	150 sccm	200/30 sccm	400 sccm
ICP Power	1000 W	1000 W	2500 W	2000 W	2500 W
RF Bias Power	5 W	20 W	0	200 W	0
Pressure	20 mTorr	25 mTorr	60 mTorr	25 mTorr	60 mTorr
Time	5 s	7 s	0.6 s	0.7 s	2 s
Etch rate	1.8 $\mu\text{m}/\text{min}$, 0.34 $\mu\text{m}/\text{cycle}$		7.8 $\mu\text{m}/\text{min}$, 0.4 $\mu\text{m}/\text{cycle}$		

For the dual-phase standard Bosch process, the etching decelerates due to insufficient removal of passivation layer at the bottoms of the holes. However, the triple-phase

modified Bosch process enables the adjustment of the parameters of the independent depassivation (Ar ion bombardment) step for mitigating ARDE. To promote ion bombardment, the RF power (and hence, the acceleration voltage of the argon ions, Figure 3.3 (b)) and the Ar ion bombardment time (Figure 3.3 (c)) were respectively increased to enhance the removal of the passivating polymers at the bottoms of the holes. As such, the etch depth increased without degrading the desired feature, particularly when using the combination of the original recipe and the HAR recipe (Figure 3.3 (d)). In another experiment, etching with the depassivation step of 1 s was performed for 1000 cycles (Figure 3.3 (e)). The remaining photoresist was still sufficiently thick under extended long ion bombardment (Figure 3.3 (f)), showing negligible pattern erosion (Figure 3.3 (g)). For the uniformity, the etching depth with a specific recipe had a standard deviation of $<5\text{ }\mu\text{m}$, showing high reproducibility.

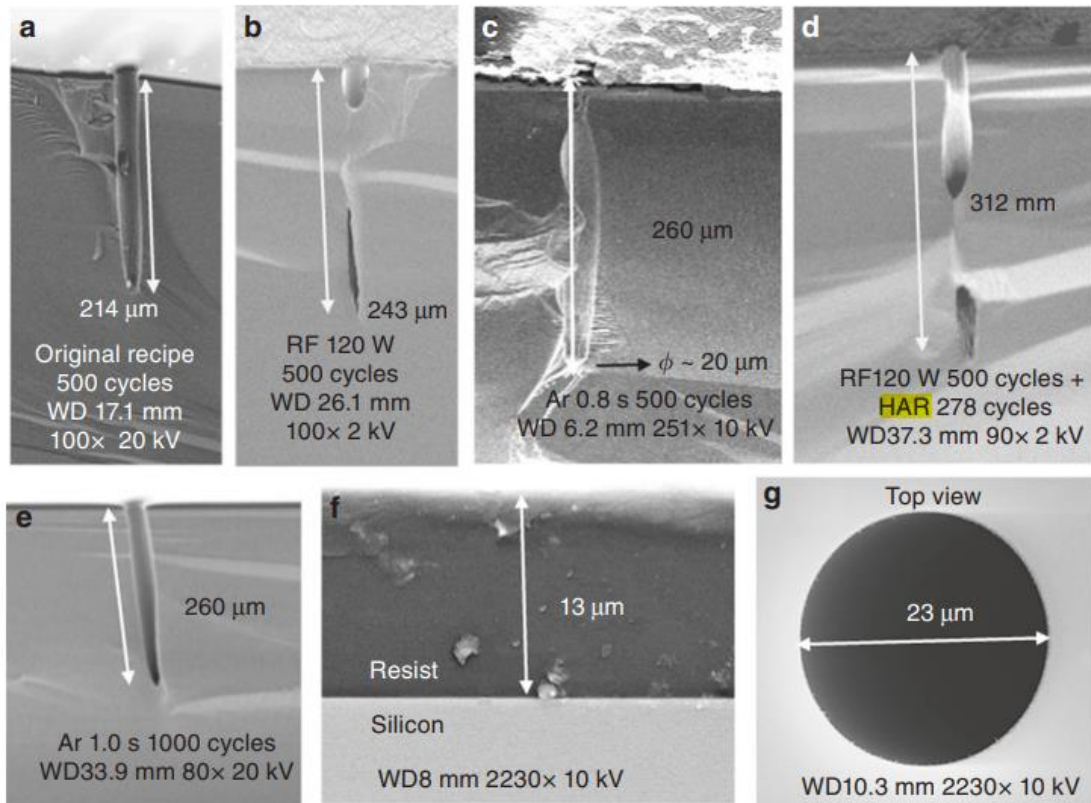


Figure 3.3 The optimization of hole DRIE etching using triple-phase modified Bosch processing.

3.3 Frontside pillar etching

For pillar etching, the standard Bosch process (listed in Table 3.1) is carried out to etch the frontside after standard photolithography with backside alignment. Unlike the etching of the holes, the etch rate doesn't decrease with an increase in the aspect ratio since the etching area is relatively large; thus, insufficient polymer removal is not an issue. 100 μm high pillars with vertical sidewalls are etched after 300 cycles of standard Bosch process (Figure 3.4 (a)), and 300 μm high pillars are etched after 900 cycles of standard Bosch process (Figure 3.4 (b)). It is observed that the 300 μm high pillars have negatively tapered profiles. The main factors causing this phenomenon are the plasma molding effect, differential charging effect, and ion scattering. For the top part of the pillar, the rounded profile was caused by resist erosion. In this project, a slight reentrant profile doesn't influence the subsequent wet etching step, and we selected 600 cycles of the standard Bosch process to etch 200 μm high pillars.

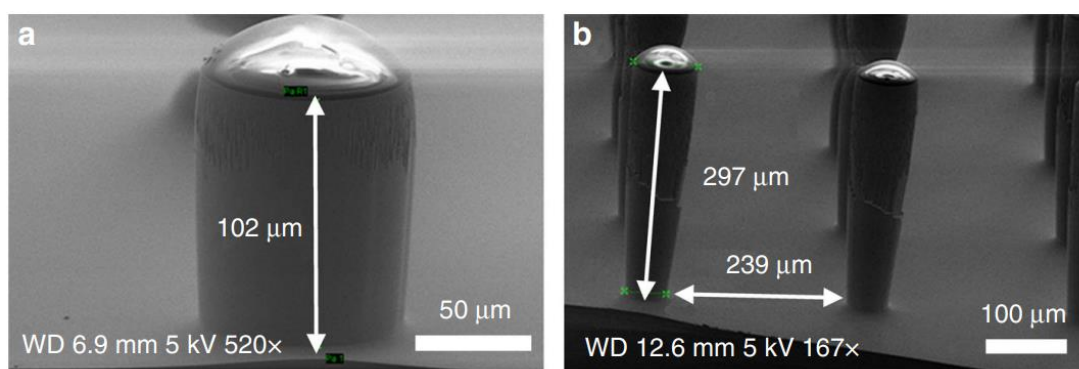


Figure 3.4 Pillar etching using standard Bosch process. (a) 300 cycles; (b) 900 cycles.

3.4 Wet etching sharpening

As discussed in Chapter 2, HF diffusion to the silicon surface is the rate-limiting factor in this reaction, since it is significantly slower than the dissolution reaction at the

surface. As a result, the HF concentration at the bottom of the pillar is much lower than that at the top of the pillar, where there is abundant silicon to consume HF fast, causing the etch rate to be much lower than that at the top, forming a cone-shaped profile. In this experiment, 1.5 cm x 1.5 cm sample piece with solid pillars after 600 cycles of standard Bosch process is placed at the bottom of the 19:1 HNO₃-HF solution in static condition. After 5 minutes of etching, the diameter of the pillar top decreases from 103 μm to 94 μm , and after 20 minutes, the pillar shrinks to 58 μm in diameter at the top, showing an etch rate of approximately 1 $\mu\text{m}/\text{min}$. After 40 minutes, the blunt tip is sharpened into a single point of less than 1 μm , while the height of the pillar shrinks to 152 μm , causing a 50 μm shrinkage (Figure 3.5). In this process, the uniformity is relatively good, with a standard deviation of less than 7.5 μm as shown in Figure 3.5(a).

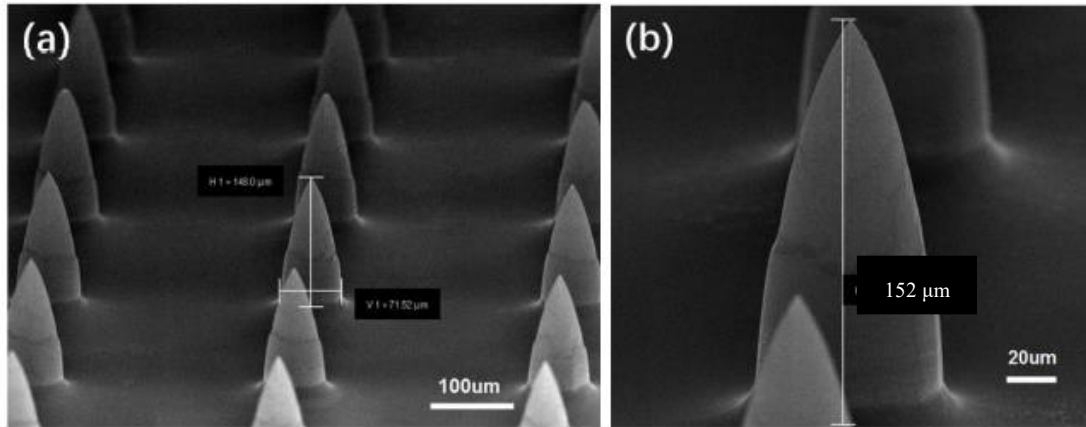


Figure 3.5 (a) SEM image for a solid silicon microneedles array with high uniformity; (b) the zoomed-in view of an individual sharp needle.

For the pillars fabricated after backside hole etching, after a 40-minute sharpening process, the off-axis hole is exposed, resulting in 160- μm high microneedles with 30- μm diameter holes positioned off-center, as shown in Figure 3.6. As shown in Figure 3.6 (a), the uniformity is also good, with a standard deviation of 2.7%.

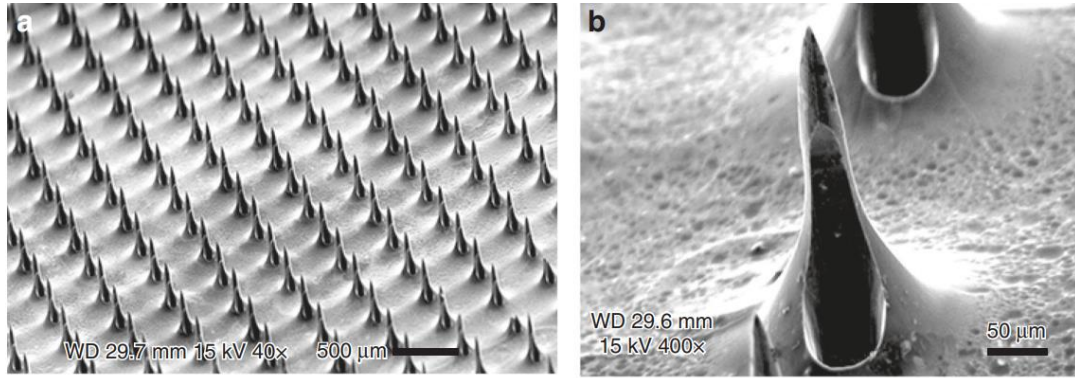


Figure 3.6 Hollow microneedles sharpened by wet etching.

However, when the pillar became taller, shortcomings (as seen below) of the HF and HNO_3 mixed wet etching were observed. We first fabricated a pillar array with a height of 300 μm, and the holes on the backside were also etched. Subsequently, the same wet etching process was performed. The etching suffers from poor reproducibility since it generates heat and increases the local temperature, which further increases the etching. Consequently, the success rate for tip sharpening was quite low (less than 40%). We also found that many factors influenced the wet etch rate, including the area of the chip, and the location of the tip. Figure 3.7 shows the results of wet etching of the 300 μm high pillars. As shown in Figure 3.7 (a), even for three consecutive pillars numbered 1, 2, and 3, the profiles of the pillars vary significantly, since not only the vertical diffusion influences the reaction, but also the lateral diffusion can influence the etch rate. Moreover, these factors are difficult to control. We attempted to change many parameters, such as the etching time and stirring conditions, but the reproducibility didn't improve. Moreover, sharpening is usually the last step of the microneedle fabrication, which results in the highest sunk cost. Therefore, to fabricate higher microneedles, we developed the process described in Chapter 4 to avoid wet sharpening.

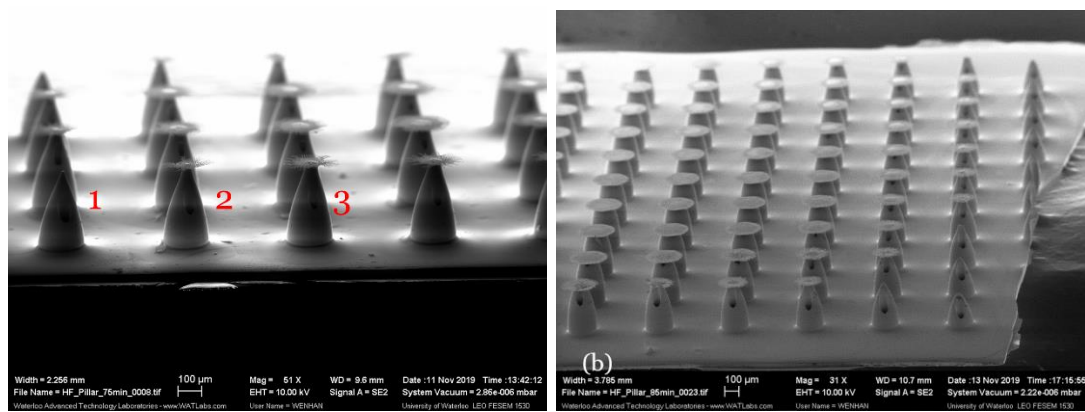


Figure 3.7 SEM micrograph of silicon out-of-plane microneedle after HF and HNO₃ mixed solution wet sharpening. The height is about 300 μ m.

Chapter 4

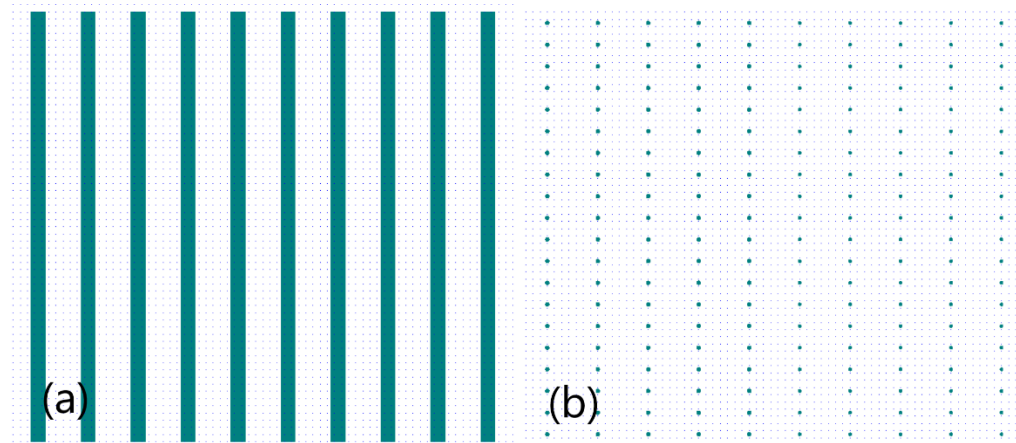
Fabrication of silicon out-of-plane hollow microneedles by DRIE and KOH etching

This chapter delineates the roadmap of our microneedle fabrication process, detailing the sequential results observed at each stage. Additionally, it elucidates the procedures involved in the optimization of the microneedle fabrication process. Moreover, it exhibits fundamental function tests of fabricated microneedles.

4.1 Overall design of silicon out-of-plane microneedles with beveled sharp tip

As mentioned in Chapter 3, utilizing the method developed in Chapter 3, it would be challenging to fabricate 600- μm high microneedles. The objective of fabricating 600- μm high microneedles is to ensure that the needle can penetrate through the epidermis and deliver the drug or extract the interstitial fluid from the dermis. Typically, fabricating cone-shaped tips presents considerable difficulties. One potential approach is KOH wet etching. However, this method has several inherent limitations. First, the microneedle density would be restricted due to the rapid lateral etch rate during KOH etching. Furthermore, the angle of the slope is determined by the crystalline plane, so an arbitrary angle cannot be obtained as desired, limiting flexibility. To address these issues, beveled tips can be formed using a two-step process: initially, fabricating a slope to form a bevel shape, followed by patterning the ring structure on the slope and etching the sample. On the backside, it is necessary to fabricate the hole structure to complete

the tunnel for drug delivery, which can be accomplished using the Bosch process. Regarding the aspect ratio, it has been determined to set it at 3, resulting in an outer diameter of 200 μm for the microneedle pillar. Consequently, the distance between the two nearest pillars on the same slope is set at 3 times the pillar diameter, which is 600 μm . For optimal microneedle density, approximately 1 needle/ mm^2 is established, resulting in a distance of 1400 μm between the two nearest pillars on the adjacent slope. The goal of this process was to fabricate a hollow silicon needle-shape array using an innovative double-sided approach. The basic logic behind our process is as follows: First, define the slope to fabricate the sharp beveled pillars. We need to fabricate slopes of approximately 200 μm high and 200 μm wide via isotropic dry etching or anisotropic wet etching before defining the hole structure on the backside of the wafer; subsequently, we define the hole structure followed by positioning the ring pillar structures on the frontside. Specifically, to make 2D repeatable structures, we can only pattern ring structures on one side of a slope. Finally, the ring pillars are etched to form the microneedles. Therefore, our process includes three essential techniques: lithography, DRIE, and isotropic or anisotropic etching. We used Clewin 4 software to complete the design of the mask pattern. Figure 4.1 shows the design of the frontside rectangular strips, frontside rings, and backside holes.



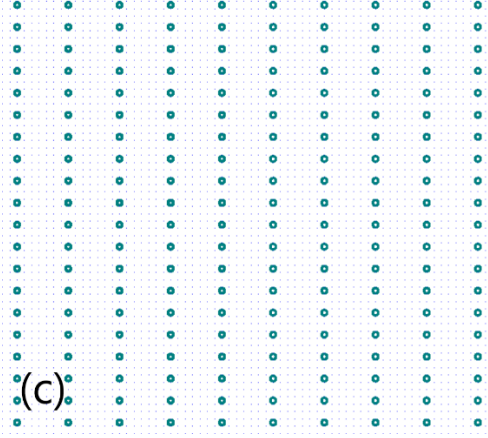


Figure 4.1 Design of the microneedle mask pattern. (a) Frontside rectangle design to fabricate the slope, the width of the rectangle is 400 μm and the length is 1.5 cm, and the gap is 1000 μm ; (b) Backside design of the microneedles, the diameter of the holes is 80-100 μm ; (c) Frontside design of the microneedles, the outer diameter of the rings is 200-240 μm and the inner diameter is 80-100 μm .

To fabricate 600- μm tall microneedles, 1 mm thick silicon wafer should be used. For the other parameters, we selected (100) boron doped 1-30 Ωcm wafer. (100) wafer was used to expose the (110) and (111) slopes. Initially, the cleaning process was carried out by HF dip and DI water rinsing, and then the wafer was immersed into acetone, followed by isopropyl (IPA) rinsing, nitrogen blowing and oxygen plasma cleaning.

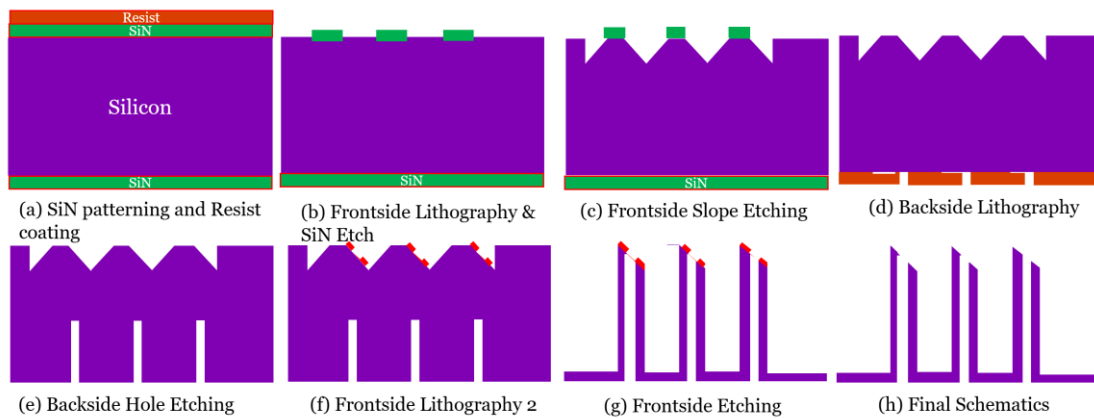


Figure 4.2 Schematic fabrication processing of hollow silicon microneedle arrays. (a) Silicon nitride coating on both sides and frontside resist coating; (b) Photolithography on the frontside and pattern transfer via silicon nitride etching; (c) Isotropic wet etching

on the front side; (d) Backside resist coating and photolithography via backside alignment; (e) DRIE on the backside; (f) Second frontside pattern on the slopes; (g) DRIE on the frontside; (h) Final schematic of the microneedle array.

As illustrated in Figure 4.2, the initial step in the fabrication process involved the deposition of silicon nitride on both sides of the wafer. This was followed by spin-coating photoresist onto the front side of the wafer. Subsequent steps included performing frontside lithography and etching the silicon nitride using RIE. Subsequently, frontside slope etching was carried out. Backside lithography via backside alignment was the next step, followed by backside hole etching using RIE. Later, frontside lithography was executed to form ring structures on the frontside slope. Then, frontside pillar etching was carried out by RIE. After the final cleaning process, a beveled tip hollow microneedle array was fabricated. In summary, the fabrication process can be categorized into three primary sectors: slope etching, backside hole etching, and frontside pillar etching.

4.2 Slope fabrication

4.2.1 Dry isotropic etching of the slope

Initially, we attempted to use dry etching to fabricate the slope. SF_6 plasma can etch silicon isotropically because, unlike C-F gases such as CHF_3 , SF_6 doesn't contain carbon and thus cannot form a sidewall passivation layer. At the same time, the plasma-generated free radical F has very low (~1%) sticking coefficient, meaning that most of it will bounce back from the sidewall or bottom to reach the area below the mask to etch the Si. In this way, we used rectangular strip shape photoresist as the etching mask. The parameters of SF_6 only etching recipe applied in Oxford Instruments PlasmaLab

System100 etcher are listed in Table 4.1. Since this recipe is directly copied from the Bosch process, there are 10 sccm C₄F₈ in the process. During Bosch process, the C₄F₈ is not fully turned off to make the switching more fluent. As shown in Figure 4.3, the sloped surface is produced after a 50-minute SF₆ etching session, resulting in a height of 200 μm.

Table 4.1 Parameters of the SF₆ only isotropic etching process with an RF frequency of 13.56 MHz.

SF₆ only Silicon Etching		
Pressure	56 mTorr	
Temperature	15 °C	
ICP Power	1200 W	
RF Bias Power	15 W	
Gas	C ₄ F ₈	SF ₆
Gas Flow	10 sccm	100 sccm
Time	50 min	
Etch Rate	4 μm/min	

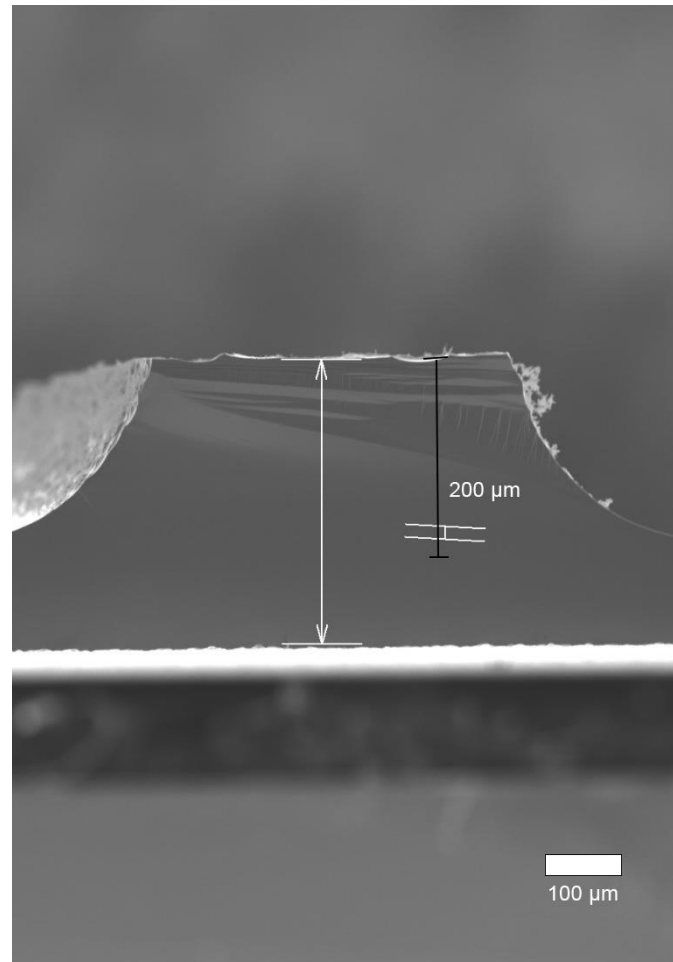


Figure 4.3 Cross-sectional SEM image of the slope after 50 minutes' SF_6 Etch. The wafer is $500\text{ }\mu\text{m}$ thick and slope is $200\text{ }\mu\text{m}$ high.

However, the shape of the slope is curved, which causes difficulties in the following steps. First, it causes difficulty in controlling the uniformity of the photoresist coating on the slope. Another problem is that the shape of the needle tip increases the risk of leakage.

4.2.2 Wet anisotropic etching of the slope

Since the slope fabricated by dry etching is not suitable for future steps, an alternative method is desired. Wet etching using potassium hydroxide can achieve anisotropic

etching.

First, 700 nm thick silicon nitride was deposited on both sides of the wafer via PECVD (HQ-8B, China). The parameters of PECVD are listed in Table 4.2. For gas selection, NH_3 can replace nitrogen gas but the ratio of silicon to nitrogen changes. LPCVD is also an alternative method for depositing silicon nitride with better film quality. In PECVD, the reaction is usually unbalanced, and thus, the etching by-product containing C and H easily enters the film as impurities. For silicon nitride films deposited by PECVD, there is usually some hydrogen in the film, and the film is not fully dense, so KOH etches PECVD silicon nitride faster than LPCVD silicon nitride. The reason we selected PECVD is that for LPCVD, it is more efficient only when a large number of wafers are to be deposited at the same time, because it requires a strict lengthy wafer cleaning process and the deposition typically takes a much longer time than PECVD. Then, a layer of AR-P5350 positive photoresist (All Resist, Germany) was spun onto the frontside of the wafer at 4000 rpm for 50 seconds, with a thickness of $\sim 1.8 \mu\text{m}$. Next, ultraviolet (UV) direct writing was carried out using a maskless aligner (MLA, Heidelberg DWL66+). The 405 nm laser power was 18 mW, and the strip length is 300 μm . Afterwards, development was performed by immersing the exposed sample in developer solution (1:7 AR 300-26 developer) for 50 seconds.

Table 4.2 Parameters of PECVD of silicon nitride deposition

SiN Deposition		
Pressure	20 Pascal	
Temperature	350 °C	
RF Power	100 W	
Gas	SiH_4	N_2
Gas Flow	24 sccm	196 sccm
Time	1500 s	
Deposition Rate	0.47 nm/s	

Subsequently, the pattern is transferred from the photoresist layer to the silicon nitride

layer with vertical sidewalls via reactive ion etching using the photoresist as the mask. The parameters for silicon nitride etching recipe are listed in Table 4.3. In this recipe, CHF_3 forms the passivation layer to ensure the vertical profile, whereas SF_6 provides abundant F free radical for silicon nitride etching.

Table 4.3 Parameter of ICP-RIE for silicon nitride etching.

SiN Etching		
Pressure	10 mTorr	
Temperature	20 °C	
ICP Power	300 W	
RF Bias Power	20 W	
Gas	CHF_3	SF_6
Gas Flow	45 sccm	15 sccm
Time	4 min	
Etch Rate	200 nm/min	

Subsequently, the wafer was cleaned using acetone and isopropyl alcohol to remove any residual photoresist. For the preparation of the KOH solution, 60 g of analytical reagent (AR) grade solid KOH was dissolved in 140 mL of deionized (DI) water to create a 30 wt.% KOH solution. This solution was heated to 85 °C in a water bath, and the wafer was immersed under static conditions for 2.5 hours. The vertical etch rate of KOH at this temperature was approximately 100 $\mu\text{m}/\text{h}$. As depicted in Figure 4.4, after 2.5 hours of etching, the slope had a height of 250 μm and a width of approximately 200 μm . The resulting slope angle was approximately 54.7°, which corresponds to the angle between the (111) and (100) planes.

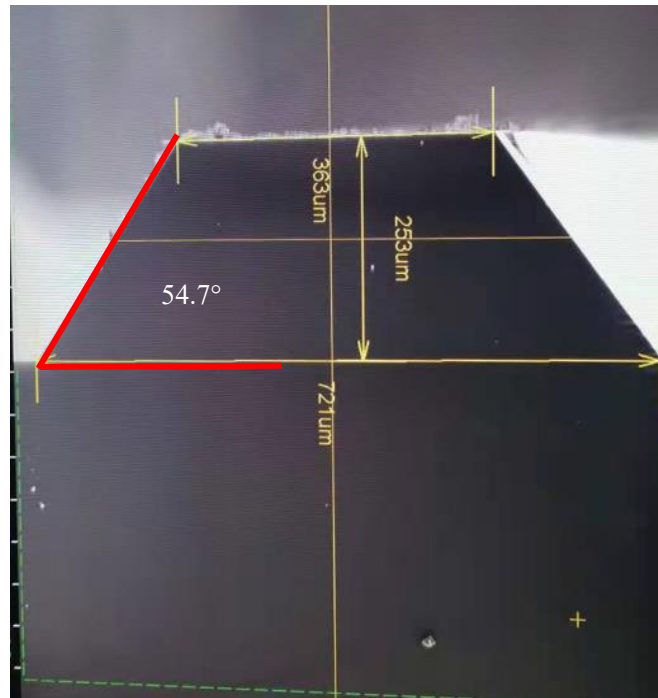


Figure 4.4 Cross-sectional SEM image of the slope after 2.5 h KOH wet etch. The slope is 250 μm high and 200 μm wide, showing a 54.7° slope.

While it is a very well-known process to fabricate slopes having 54.7° , 45° slope is also possible if the original mask pattern sides are aligned with the (010) direction in order to show up the (011) slope, instead of the popular (111) slope when the mask pattern sides are aligned along the (110) direction. The prerequisite for forming the 45° (011) slope is that its etching rate must be the local minimum, notably slower than that of (001) plane, which is unfortunately not the case for KOH or TMAH etching if without a surfactant.

As such, for 45-degree slope etching, an additional ~ 80 mL of IPA surfactant was added to the solution to saturation in order to greatly slow down the etching rate of the (110) plane with little effect on the (100) plane etching rate. As shown in Figure 4.5, phase separation was readily observed in the solution with the excess IPA floating at the top. The motivation to fabricate 45° is that, for 54.7° slope, it is still not easy to perform the alignment in the next photolithography step, so that 45° is a balanced angle between sharpness and difficulty of alignment. Moreover, 45° slope fabrication can ensure that our design can be customized to meet different demands.

The solution was heated to 75 °C by water bath, and the wafer was immersed to the solution. After 2 h of wet etching, the sample was examined using SEM imaging. As shown in Figure 4.7, the slope had 100 μm width and 100 μm depth, showing that the slope angle is 45°, complying with the angle between the (110) and (100) planes.

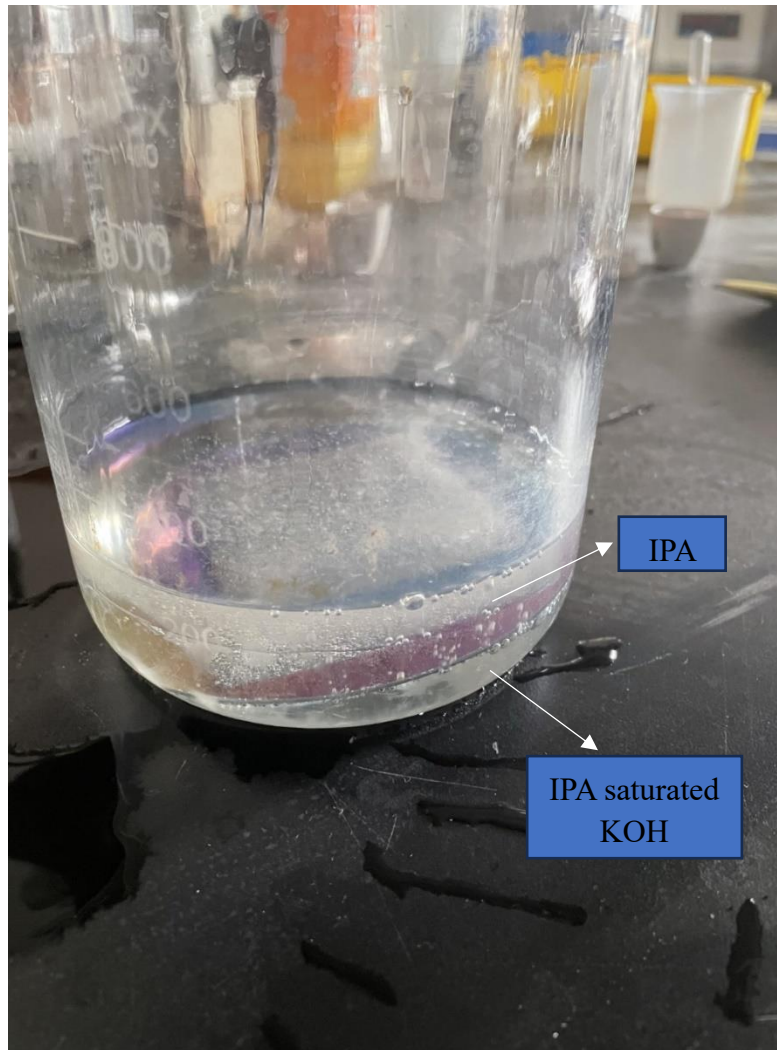


Figure 4.5 Phase separation of KOH-IPA saturated solution.

As shown in Figure 4.6, the etch rate of KOH with saturated IPA at 75 °C was 50 $\mu\text{m}/\text{h}$. Consequently, 4 h etching was performed, and the slope was 200 μm in height and 200 μm in width. Figure 4.7 shows the SEM image of the slope and Figure 4.8 shows the sample after etching. We observed that the sample was not clean and smooth. The SEM image shows multiple small pyramid-shaped hills on the surface (such as the circled

part in Figure 4.7 and Figure 4.8). This is because the native oxide on the silicon wafer acted as an etching mask. Compared to the situation of 54.7° slope etching, the etch rate dropped by 50%, which also lowered the etch rate of native oxide film on the surface of the wafer, causing an unsmooth surface. Fortunately, this did not influence the subsequent etching process.

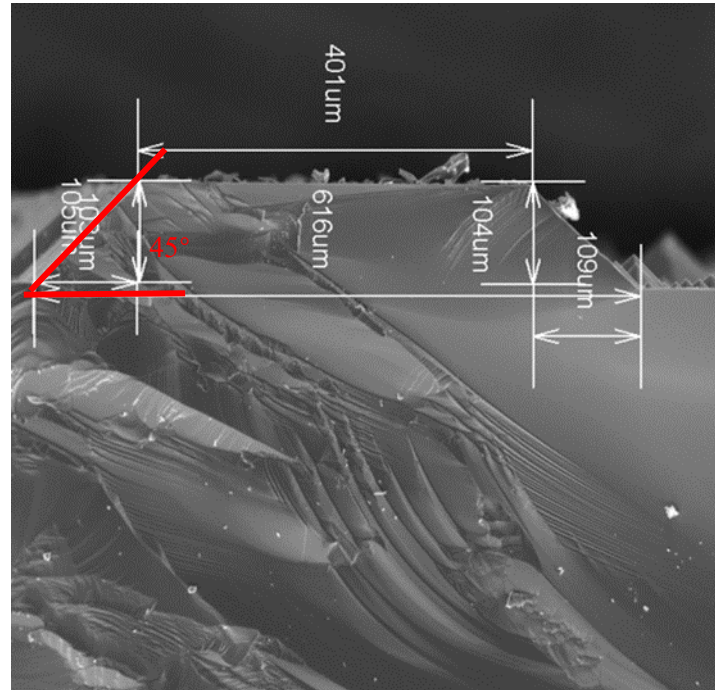


Figure 4.6 Cross-sectional SEM image of 45° slope after 2 h wet etching by KOH with saturated IPA.

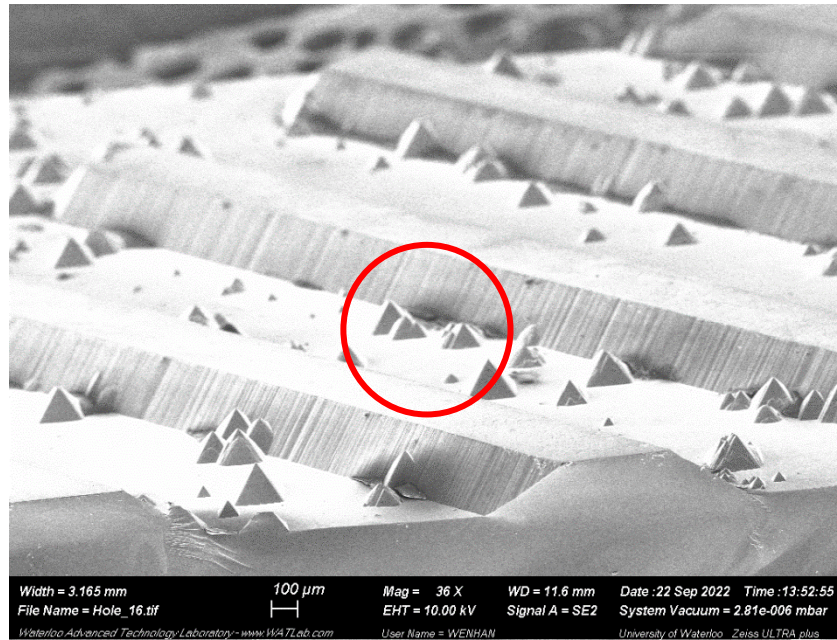


Figure 4.7 SEM image of 45° slope after 4 h wet etching by KOH with saturated IPA.

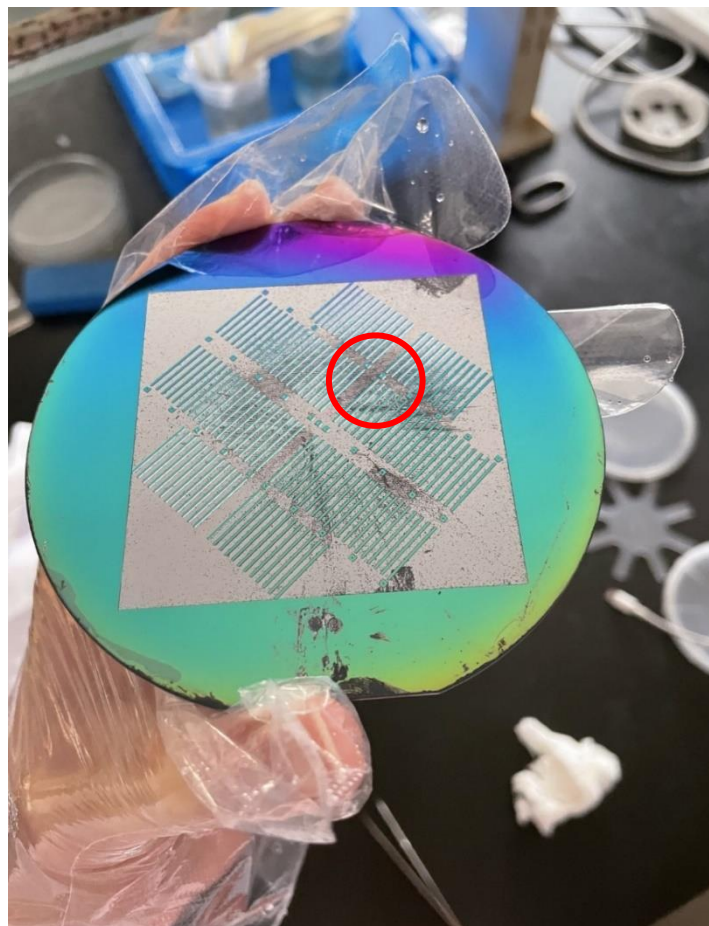


Figure 4.8 Image of the sample after 4 h wet etch using KOH with saturated IPA.

In addition to KOH, TMAH can also complete isotropic etching of silicon, exposing the (111) or (110) plane. Although TMAH has a relatively lower etch rate than KOH, one advantage for TMAH over KOH is that for TMAH etching, both silicon oxide and silicon nitride can work as etching masks since TMAH etches silicon oxide roughly 90% slower than KOH, while only silicon nitride is the proper etching mask for KOH etching. Consequently, for the TMAH etching sample, the etching mask is 300 nm thick thermal oxide. Besides, Triton X-100 was added to the solution as a surfactant to slow the etch rate of (110) to less than the rate of (100).

For 54.7° sample, the mask design is the same as KOH sample. The solution contained 25% TMAH + 0.01% Triton X-100. We also used a water bath to heat the solution to 85 °C, and to remove the influence of native oxide, we immersed the wafer to 1:10 BOE for 10 s and after that the wafer was immersed to the solution immediately for wet etching. The vertical etch rate was 41 µm/h, and 246 µm slope was fabricated after 6 h of wet etching with the slope angle of 54.7° (Figure 4.9), complying with the angle between the (111) and (100) plane. In addition, the surface was quite smooth without small pyramid hills.

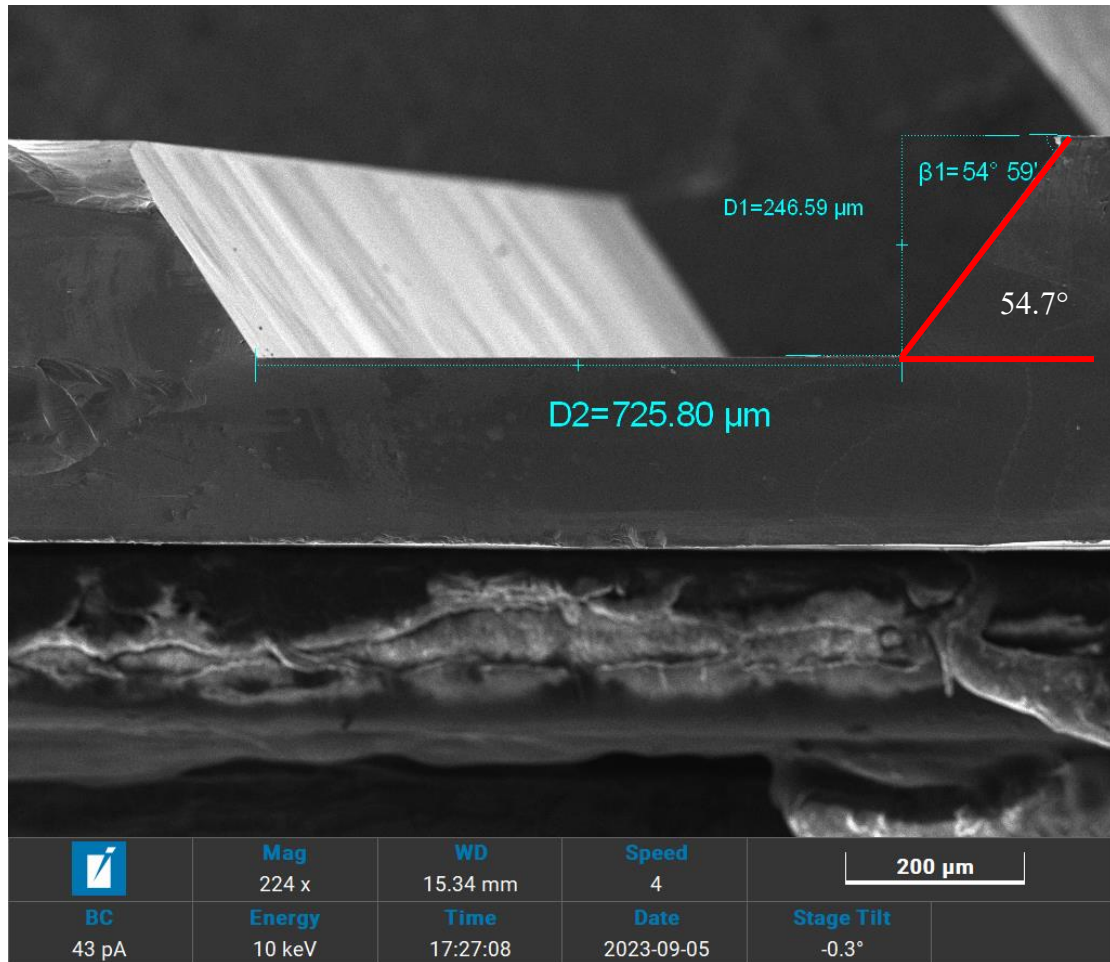


Figure 4.9 Cross-sectional SEM image of 54.7° slope fabricated by TMAH with Triton X-100.

For 45° slope, similar to the KOH condition, the pattern should be rotated 45° ensuring that the short side of the rectangle is perpendicular to the flat side of the wafer. The solution contained 25% TMAH + 0.01% Triton X-100. A water bath was also used to heat the solution to 85 °C, and wafer was immersed to the solution for wet etching right after 10 s of 1:10 BOE process. The vertical etch rate was 44 μm/h, and 220 μm slope was fabricated after 5 h wet etching with the slope angle of 45° (Figure 4.10). Table 4.4 summarizes the four situations discussed above, and we can see that all these methods are suitable for slope etching.

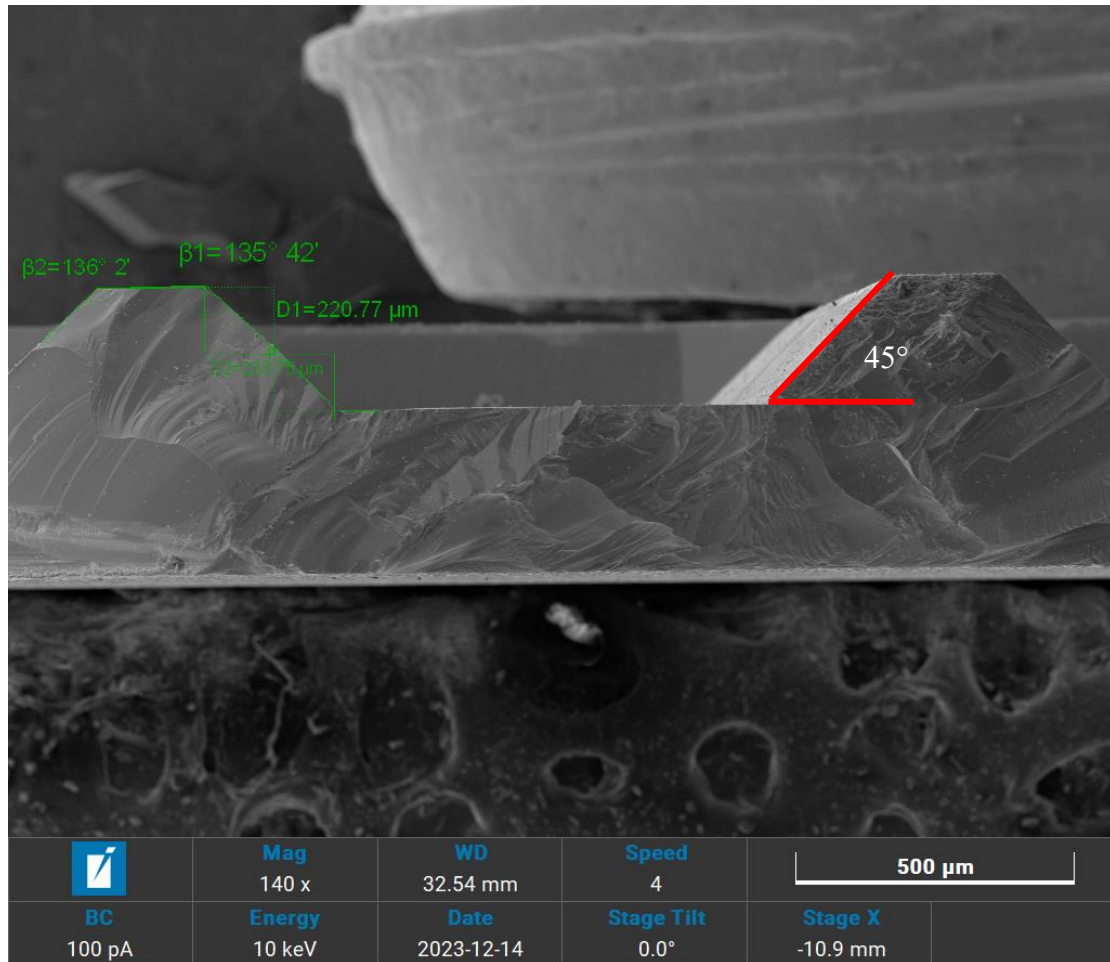


Figure 4.10 Cross-sectional SEM image of 45° slope fabricated by TMAH with Triton X-100

Table 4.4 Summary of four different wet etching methods to fabricate slope.

	Etch mask	Pattern rotation	Vertical Etch rate (μm/h)	Slope angle	Surface roughness
30% KOH	SiN (PECVD)	No rotation	100	54.7°	Smooth
30% KOH with saturated IPA	SiN (PECVD)	45° rotation	50	45°	Rough (No pretreatment by BOE)
25% TMAH + 0.01% Triton X-100	SiO ₂ (Thermal)	No rotation	41	54.7°	Smooth (Pretreated by BOE)

25% TMAH	SiO ₂	45°	41	45°	Smooth
+ 0.01% Triton X-100	(Thermal)	rotation			(Pretreated by BOE)

4.3 Backside hole etching

As discussed in Section 3.2, ARDE is a challenging part of hole etching. Moreover, we need to etch holes with a depth of $\sim 500\ \mu\text{m}$ and a diameter of $80\text{-}100\ \mu\text{m}$, which is quite difficult using Standard Bosch recipe. We tested several samples with $60\ \mu\text{m}$ diameter holes and found that after 700 cycles of Standard Bosch recipe (Table 4.5), the etch rate was extremely low (almost 0). At that time, the depth of the holes was only about $320\ \mu\text{m}$ (Figure 4.11). Consequently, a revised Bosch recipe was proposed. Since the main reason for ARDE in the hole etching process is insufficient passivation layer removal during the etch cycle, therefore, the revised recipe incorporates an extended etch sub-cycle. As detailed in Table 4.6, the etch sub-cycle time was increased from 5 seconds to 7 seconds. While the ideal method is to ramp up the etch sub-cycle time, however, owing to equipment limitations, we can only use the combination of Standard Bosch recipe and Revised Bosch recipe. Specifically, for the first 700 cycles, we etch the holes using Standard Bosch recipe; after that, Revised Bosch recipe is adapted to etch deeper. Figure 4.11(b) illustrates the results after applying 700 cycles of Standard Bosch recipe and 600 cycles of Revised Bosch recipe, achieving a hole depth of $452\ \mu\text{m}$.

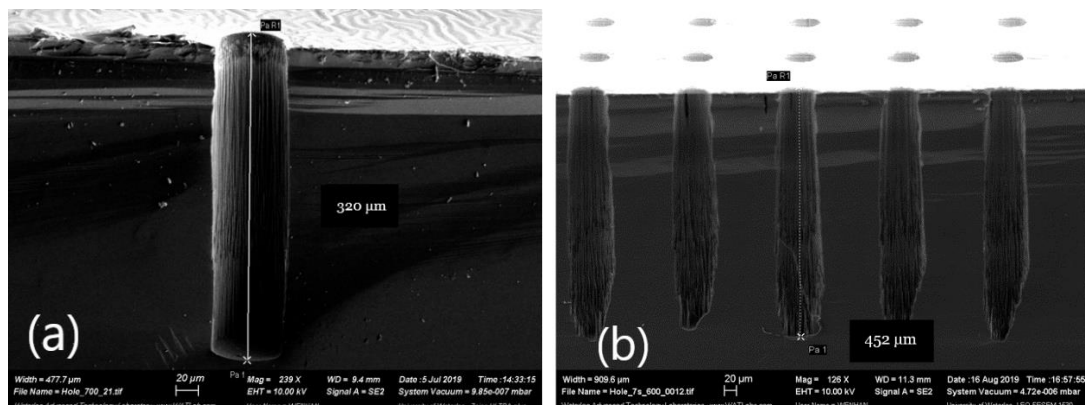


Figure 4.11 SEM image for the holes (a) after 700 cycles of Standard Bosch recipe, the depth is 320 μm , the diameter is 60 μm ; (b) after 700 cycles of Standard Bosch recipe and 600 cycles of Revised Bosch recipe, the depth is 320 μm and the diameter is 60 μm .

Table 4.5 Parameters of the Standard Bosch Process recipe for hole etching on Oxford PlasmaPro Cobra 100 in CIRFE Lab (Bosch process) with an RF frequency of 13.56 MHz at 0 °C.

	Passivation		Etch	
Gas	C ₄ F ₈	SF ₆	C ₄ F ₈	SF ₆
Flow	180 sccm	5 sccm	5 sccm	400 sccm
ICP Power	1500 W		1800 W	
RF bias Power	5 W		15 W	
Time	2 s		5 s	
Pressure	25 mTorr		40 mTorr	

Table 4.6 Parameters of the Revised Bosch Process recipe for hole etching on Oxford PlasmaPro Cobra 100 in CIRFE Lab (Bosch process) with an RF frequency of 13.56 MHz at 0 °C.

	Passivation		Etch	
Gas	C ₄ F ₈	SF ₆	C ₄ F ₈	SF ₆
Flow	180 sccm	5 sccm	5 sccm	400 sccm
ICP Power	1500 W		1800 W	
RF bias Power	5 W		15 W	
Time	2 s		7 s	
Pressure	25 mTorr		40 mTorr	

Due to the COVID-19 pandemic, later, we used Oxford Instruments PlasmaLab System100 etcher at Zhejiang University, China. We developed a similar method for etching the holes. As shown in Table 4.7, a three-phase Bosch process was adapted. In this recipe, RF bias power is not necessary for the two passivation steps since fluorocarbon polymer deposition doesn't rely on RF bias power. The reason for keeping

the RF bias power on is to increase the stability of the process since this can help the recipe transfer from etching to passivation 1 step smoothly. We etch holes with 80-100 μm diameter to 500 μm deep. Figure 4.12 shows the results of the holes etched at Zhejiang University.

Table 4.7 Parameters of the DRIE etching process for backside hole etching (Bosch process) with an RF frequency of 13.56 MHz at 15 °C.

	Passivation 1	Passivation 2	Etching
ICP Power	900 W	700 W	1000 W
Cycle	2 s	3 s	6 s
Gas	C ₄ F ₈	C ₄ F ₈	SF ₆
Flow rate	100 sccm	100 sccm	100 sccm
RF Bias Power	15 W	6 W	15 W
Pressure	30 mTorr	30 mTorr	40 mTorr
Etch rate	0.25 $\mu\text{m}/\text{cycle}$, 1.4 $\mu\text{m}/\text{min}$		

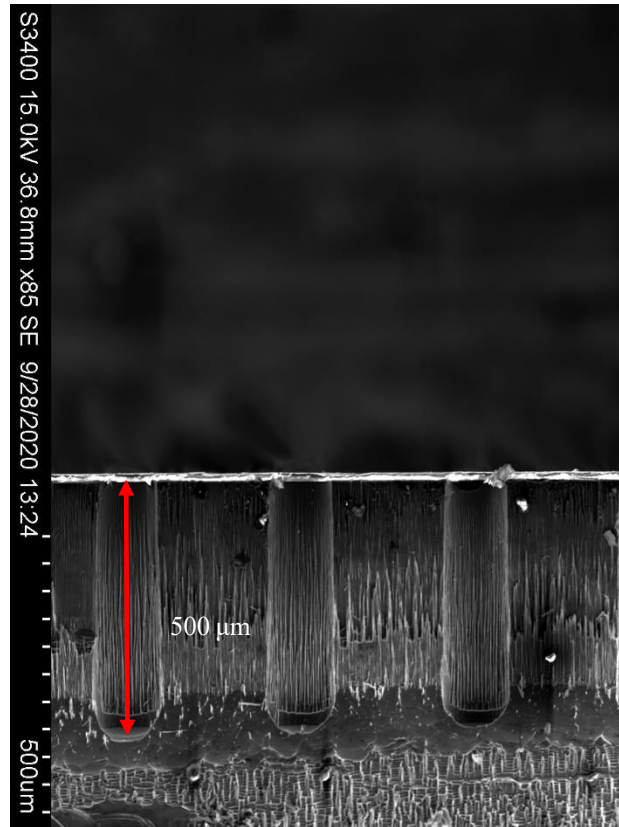


Figure 4.12 SEM image of the holes after DRIE in Zhejiang University. The depth is about 500 μm and the diameter is 80 μm .

4.4 Frontside lithography

After the hole etching, standard cleaning was performed to remove the remaining resist on the frontside. The photoresist was then coated on the frontside by spray coating. At first, we attempted to use spin coating to coat the photoresist. However, as illustrated in Figure 4.13, the post-photolithography uniformity of the resist thickness was suboptimal. The resist layer on the slope was notably thin, leading to rapid etching away of this region and consequently causing failure during the frontside pillar etching process. Therefore, spray coating was adopted to ensure a more uniform resist application.

In spray coating, the resist film is deposited from an atomized photoresist with typical droplet sizes in the μm range. The droplets are formed via a nitrogen-filled nozzle

similar to conventional air brush guns, and land on the substrate surface carried by an air or nitrogen flow to increase the dropping speed and density of the droplet where they combine to form a continuous resist film. Spray coating offers the potential to coat arbitrarily shaped substrates in which spin-coating is not technically feasible or does not provide the results required with respect to the homogeneity and edge coverage of the resist film over texture¹¹⁴, for instance, sidewalls and slopes, corresponding to our situation.

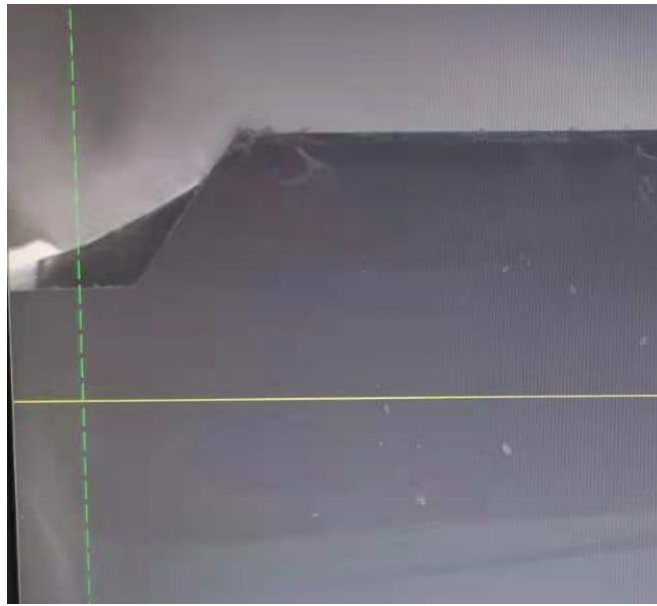


Figure 4.13 Profile of spin-coated photoresist (HTF-4025G, Hantop, China) after frontside photolithography.

For the photoresist selection for spray coating, two types of negative photoresists have been used. One resist is ROL-7133 (RDMicro, China), which can form a 10 μm thick film. The other is SUN-9i (Semicon, China), which can form ~ 12 μm thick film with acceptable uniformity (Figure 4.14). For SUN-9i coating, we first diluted the photoresist with PGMEA at 1:4 to reduce the viscosity of the photoresist to generate small droplets during the spray coating process. The viscosity of the photoresist must be well controlled. A viscosity that is too low would lead to resist flowing, resulting in poor edge coverage, while a viscosity that is too high would lead to an unsmooth film profile. The nozzle height was 40 mm from the wafer surface and the spacing between

the nozzles was 2 mm. The scanning speed for the nozzle was 200 mm/s and five scans were processed for the entire coating to complete a uniform film. The temperature of the photoresist was 100 °C. This is because it is important to evaporate some solvent during the flight from the spray nozzle to the substrate, and the hereby increased resist viscosity prevents the resist from macroscopically converging on the substrate and withdrawing from the edges of textures¹¹⁴. However, if too much solvent is evaporated, it would be difficult for the photoresist to stick to the substrate since resin particles would be formed during flight.

The pressure of the photoresist droplet was maintained at 0.18 MPa, with a flow rate of 1.5 mL/min. The nitrogen flow pressure was set to 0.2 MPa. A subsequent soft bake was performed at 110 °C for 90 seconds, resulting in a film thickness of 9-13 μm on the slope. This method demonstrated superior uniformity compared to the spin coating process.

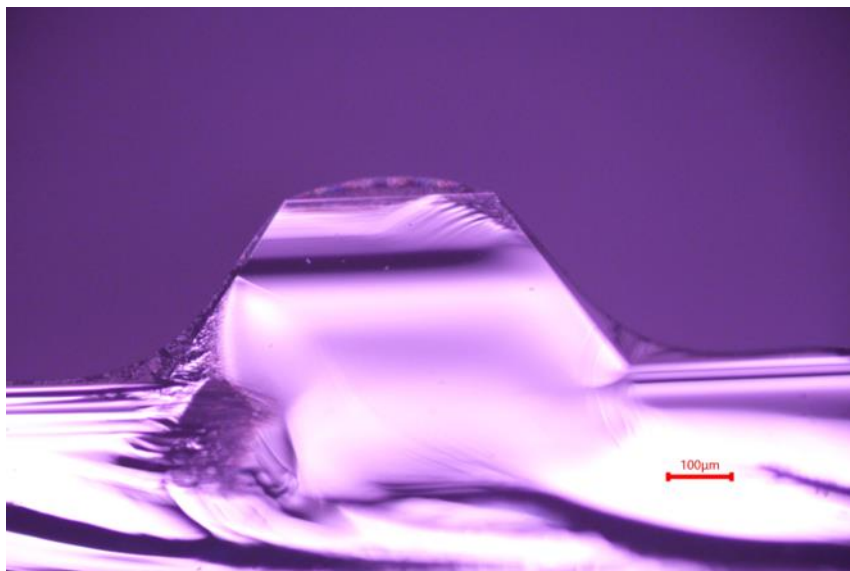


Figure 4.14 Cross-sectional microscopy image of 54.7° slope with spray coated SUN-9i negative photoresist.

After spray coating, standard photolithography was performed using SUSS-MA6 mask aligner. The alignment markers were on the backside of the wafer, and we completed the backside alignment via SUSS-MA6 mask aligner.

Due to the existence of the slope, there is a 200- μm height difference on the frontside, which completely exceeds the depth of field limit for MLA. Thus, the mask aligner was the sole option for lithography. Moreover, this step is quite challenging since the alignment markers also have 200 μm height difference, making it difficult to focus during alignment. It is not possible to see the marker and substrate clearly at the same time, and we can only use the light spot at the center of the marker to complete the alignment (Figure 4.15).

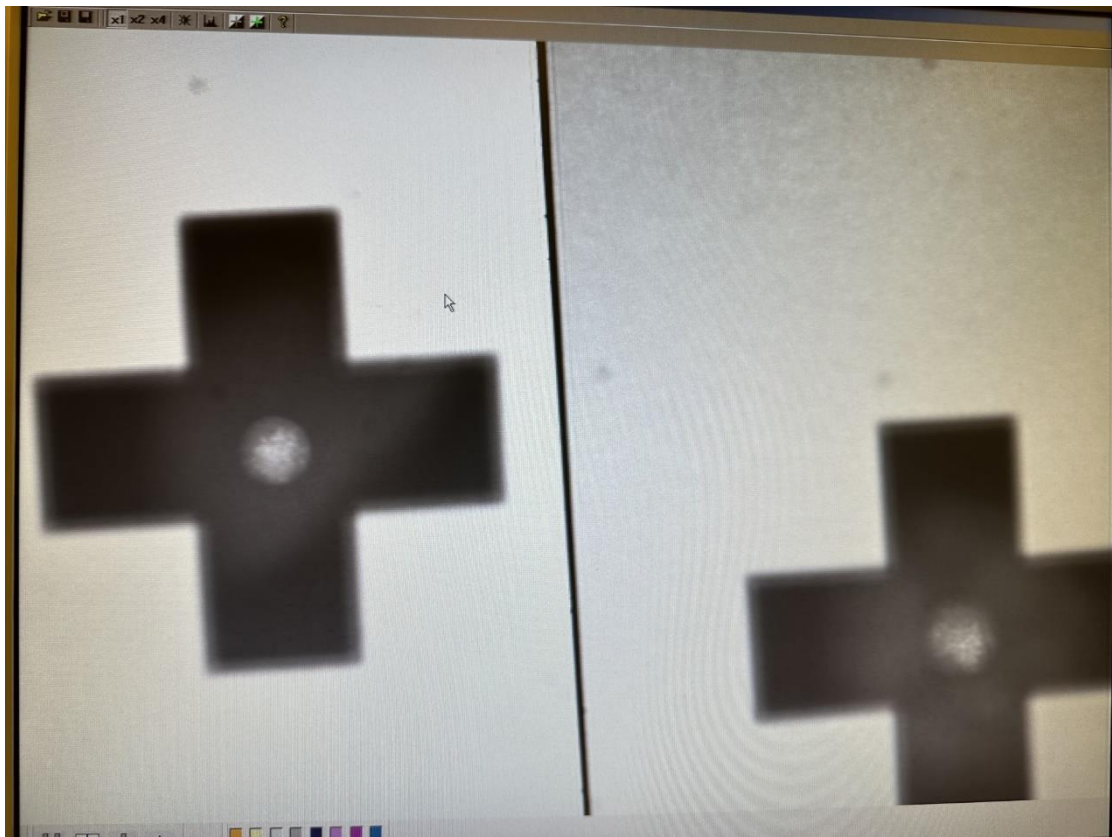


Figure 4.15 Frontside alignment during frontside photolithography on the slope.

The exposure dose for both the photoresists was 120 mJ/cm^2 . After exposure, post exposure bake was processed on 110°C hot plate for 90 s, and standard development was implemented using 2.38% TMAH for 7 min afterwards. As shown in Figure 4.16 and Figure 4.17, it can be confirmed from the microscopy and SEM image that the photolithography is successful.

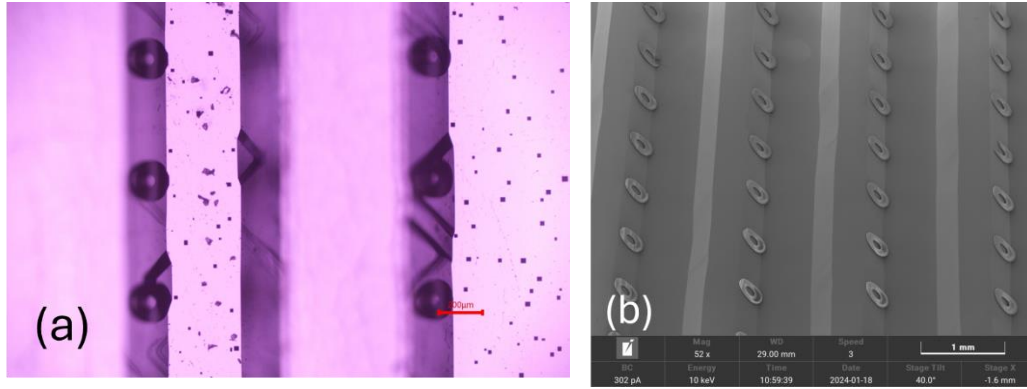


Figure 4.16 Frontside ring structures after photolithography on 54.7° slope using SUN-9i photoresist. (a) Top view of microscopy image of ring structures; (b) SEM image of ring structures.

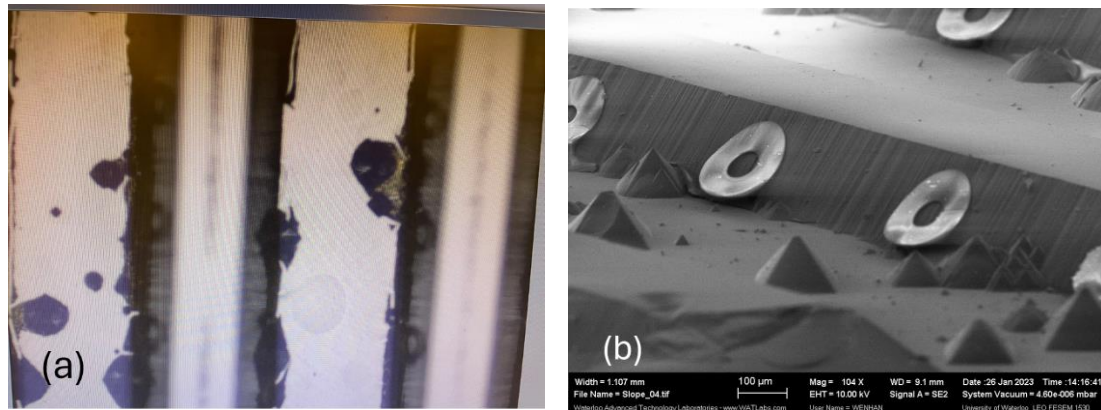


Figure 4.17 Frontside ring structures after photolithography on 45° using ROL-7133 photoresist. (a) Top view of microscopy image of ring structures; (b) SEM image of ring structures.

4.5 Frontside pillar etching

For frontside pillar etching, ARDE would not be a problem due to the low aspect ratio dependency; the biggest challenge is the negatively tapered profile. In Chapter 3, when we attempted to fabricate 300 μm high microneedles, we found an undercut profile which could not be ignored (Figure 4.18). Since the standard Bosch can form a vertical profile when etching the holes, the passivation layer removal would be too high for

pillar etching. Even worse, the thickness of the ring structure in the microneedles was only about 50 μm , while the height was 500 μm , thus a 5° negative slope would cause destructive shrinkage at the pillar bottom part. Consequently, another revised Bosch recipe is proposed.

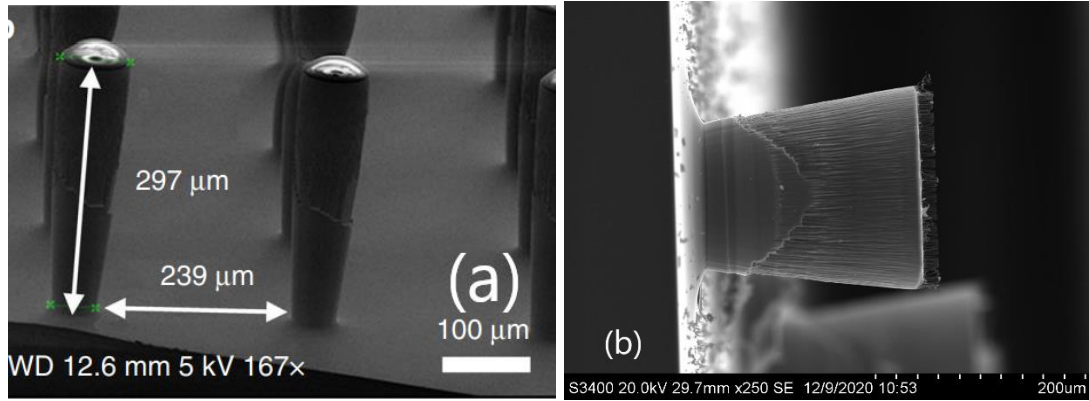


Figure 4.18 SEM photograph for etched pillars. (a) Pillars etched via standard Bosch recipe in Quantum NanoFab, the height is 297 μm with apparent negative tapered profile. (b) Pillars etched via Bosch Processing in Oxford PlasmaPro100 ICP-350, the height is 200 μm with apparent negative tapered profile.

Finally, we chose an easy method using a powerful etcher which can control the profile of the sidewall well, such as Oxford Estrelas 100 ICP-RIE in nanoFAB, University of Alberta, and Samco RIE-iPB800 in Tanwei Nanotechnology.

The etching recipes for Bosch process are presented in Table 4.8 and Table 4.9. In this section, we divide the typical etching process into two steps: breakthrough and etching. The main purpose of the breakthrough step was to remove the passivation layer at the bottom by ion bombardment. In this way, RF bias power should be relatively high to achieve a sufficient removal process. The time of the breakthrough step should be well controlled; if the time is too short, the passivation layer removal would not be completed, significantly reducing the etch rate, while too long breakthrough step would cause the passivation layer removal on the sidewalls, leading to isotropic profile (negatively tapered profile for pillars). In addition, the ion bombardment is a physical process, and it will etch both silicon and the etching mask, so a long breakthrough will

decrease the selectivity of silicon and etching mask. Since the mechanism of SF₆ etching is a free radical dominance process, there is no need to add RF bias power in the etching step (that follows the breakthrough step).

Table 4.8 Parameters of the DRIE high rate etching process on Oxford Estrelas 100 with an RF frequency of 13.56 MHz at 5 °C.

	Passivation	Breakthrough	Etching
ICP Power	2500 W	2500 W	2500 W
Cycle	1 s	1 s	3 s
Gas	C ₄ F ₈	SF ₆	SF ₆
Flow rate	150 sccm	200 sccm	400 sccm
RF Bias Power	0 W	100 W	0 W
Pressure	60 mTorr	25 mTorr	60 mTorr
Etch rate	0.6 µm/cycle, 10.8 µm/min		

Table 4.9 Parameters of the DRIE etching process on Samco RIE-iPB800 with an RF frequency of 13.56 MHz at -10 °C.

	Passivation	Breakthrough	Etching
ICP Power	1600 W	750 W	2000 W
Cycle	2.5 s	2 s	3 s
Gas	C ₄ F ₈	SF ₆	SF ₆
Flow rate	200 sccm	100 sccm	100 sccm
RF Bias Power	0 W	600 W	0 W
Pressure	15 mTorr	12 mTorr	38 mTorr
Etch rate	0.6 µm/cycle, 4.8 µm/min		

However, considering the current equipment, we also developed a novel method to fabricate the ring pillars with vertical sidewalls, which will be introduced in the next section.

4.5.1 Frontside pillar etching optimization: sacrificial structures

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Wenhan Hu, Zihao Wang, Aixi Pan, Bo Cui, “High aspect ratio silicon ring-shape micropillars fabricated by deep reactive ion etching with sacrificial structures,” Micro and Nano Engineering, Volume 22, 2024, 100234, ISSN 2590-0072, <https://doi.org/10.1016/j.mne.2023.100234>.

4.5.1.1 Motivation

For our microneedles, the distance between the two nearest needles in a row is 1400 μm and the distance between the two nearest needles in a column is 600 μm , which are long distances compared to typical MEMS structures.

However, a critical issue of Bosch process is that, when etching large open area, negative profile would be resulted¹¹⁶, making it difficult to fabricate high aspect ratio ring pillars. It is believed to be very challenging to control the profile at heights of several 100 μm for features with large gaps, since the plasma sheath starts to follow the etched features and the ions will deviate from normal incidence to give more serious undercut etching¹¹⁷. This plasma molding effect has been utilized for advantage for etching tilted structures next to a tall structure that “bends” the ion trajectory^{118,119,120}. Another factor that contributes to negative profile etching is the distribution of ion arrival angle caused mainly by ion-scattering along its path inside the sheath¹²¹. Differential charge is also an important factor contributing to negative profile etching, which leads to the dispersion of monodirectional ion flux^{122,123}. As shown in Figure 4.19, severe lateral etching would happen when etching widely-spaced structures,

making it negatively tapered. Typically, the profile angle can be improved by increasing the passivation half-cycle time in Bosch process¹²⁴. However, this will greatly reduce the etch rate and selectivity; and for our ring-shaped pillar structure, the etching of the hole inside the pillar will become even more difficult because of the aspect-ratio-dependent etching (ARDE) effect. That is, for high aspect ratio ring etching, the outer pillar sidewall tends to be negatively tapered, whereas the inner hole sidewall tends to be positively tapered; and effort to improve the outer surface profile angle would generally worsen the inner hole sidewall angle. ARDE effect refers to the greatly reduced etch rate with increasing aspect ratio for hole or trench etching, and the etching may even completely stop at certain high aspect ratio. It is believed to be caused by ion shadowing effect and/or reduced transport of etching species to the hole/trench bottom^{125,122}. For DRIE, an increase of the passivation time would aggravate ARDE since the removal of fluorocarbon polymer by ion bombardment at the bottom of the hole would be more difficult for higher aspect ratio. Ion bombardment can be enhanced by boosting the RF bias power, but at the cost of reduced etch rate selectivity and more negative taper angle for the pillar etching.

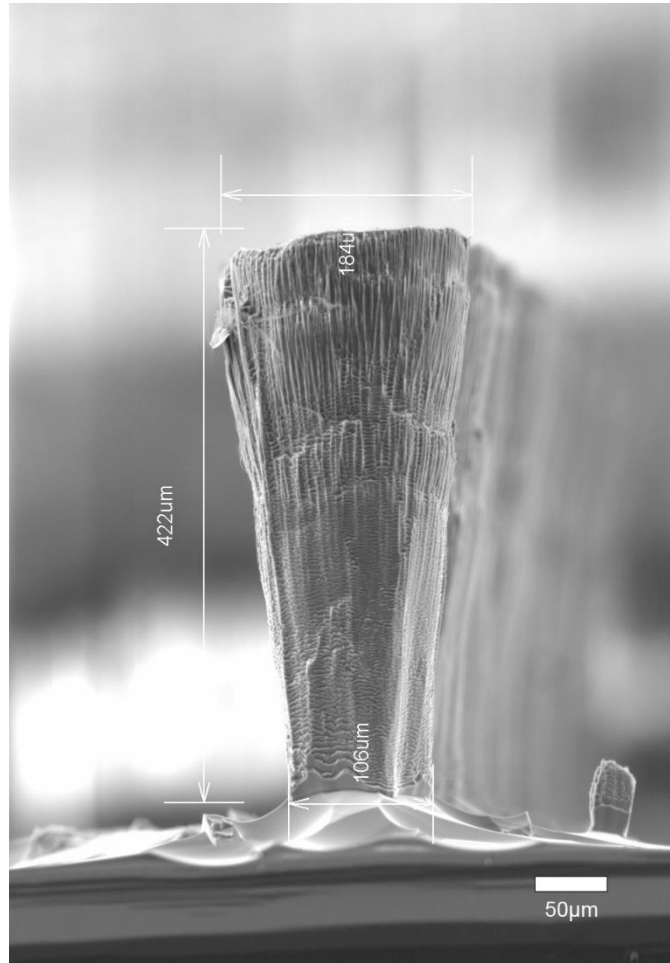


Figure 4.19 An example of lateral etching during DRIE for etching widely-spaced micro-pillars.

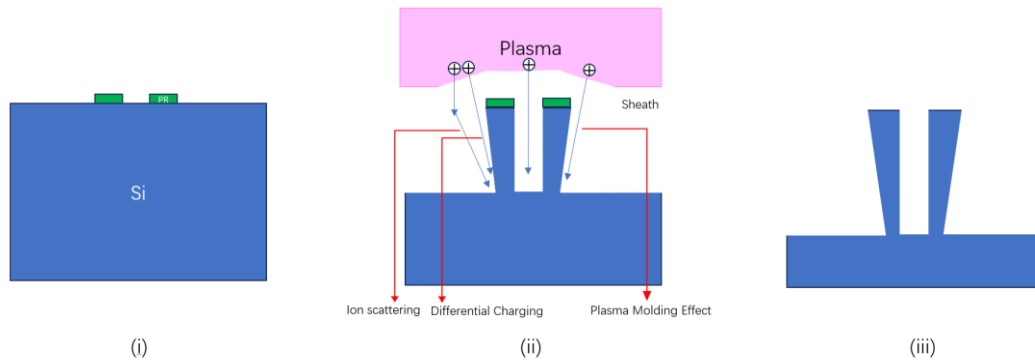
4.5.1.2 Sacrificial structures design

As introduced in the previous section, there are several factors contributing to lateral etching including ion scattering, differential charging, and plasma molding effect (Figure 4.20 (a-i,ii,iii)). Consequently, an alternative method is desired, and here adding sacrificial circular structures surrounding the ring-shaped pillars are proposed. Those surrounding structures can protect the sidewall of the pillars from lateral etching, ensuring a vertical sidewall for adequate mechanical strength. At the same time, since now the sacrificial structure is exposed to the bulk plasma and thus experience severe lateral etching, it is thinned down and could be removed during or after the etching

process, leaving behind the desired ring-shaped pillars with nearly vertical sidewall (Figure 4.20 (a-iv,v,vi)).

The designed pillar is 450 μm high and 200 μm outer diameter. The hole, patterned at the center of the pillar to form the ring shape, has an 80 μm diameter. The pillars form a 2D array with 600 μm row spacing and 1400 μm column spacing, whose parameters are same as our chip design.

As shown in Two different kinds of sacrificial structures were designed using Clewin 4 layout editor. Figure 4.20 (b) and (c) shows the design and parameters of the structures: (i) circular ring structure; (ii) two half-circle structures with two small gaps ($\sim 20\ \mu\text{m}$ wide) between them. For the latter design, we had anticipated that, when the lower part of the sacrificial ring structure is etched through due to lateral etching, the two half-sections would tend to fall away from the pillar rather than toward it; or it would be easier to break off by ultrasonic agitation since the two half circles are disconnected. However, as will be shown in the next section, with the help of ultrasonic agitation, the advantage of the second design over the first one is not significant for the present design and experiment conditions. For the same reason, we did not attempt to divide the sacrificial circles into more sections due to their easy removal after etching.



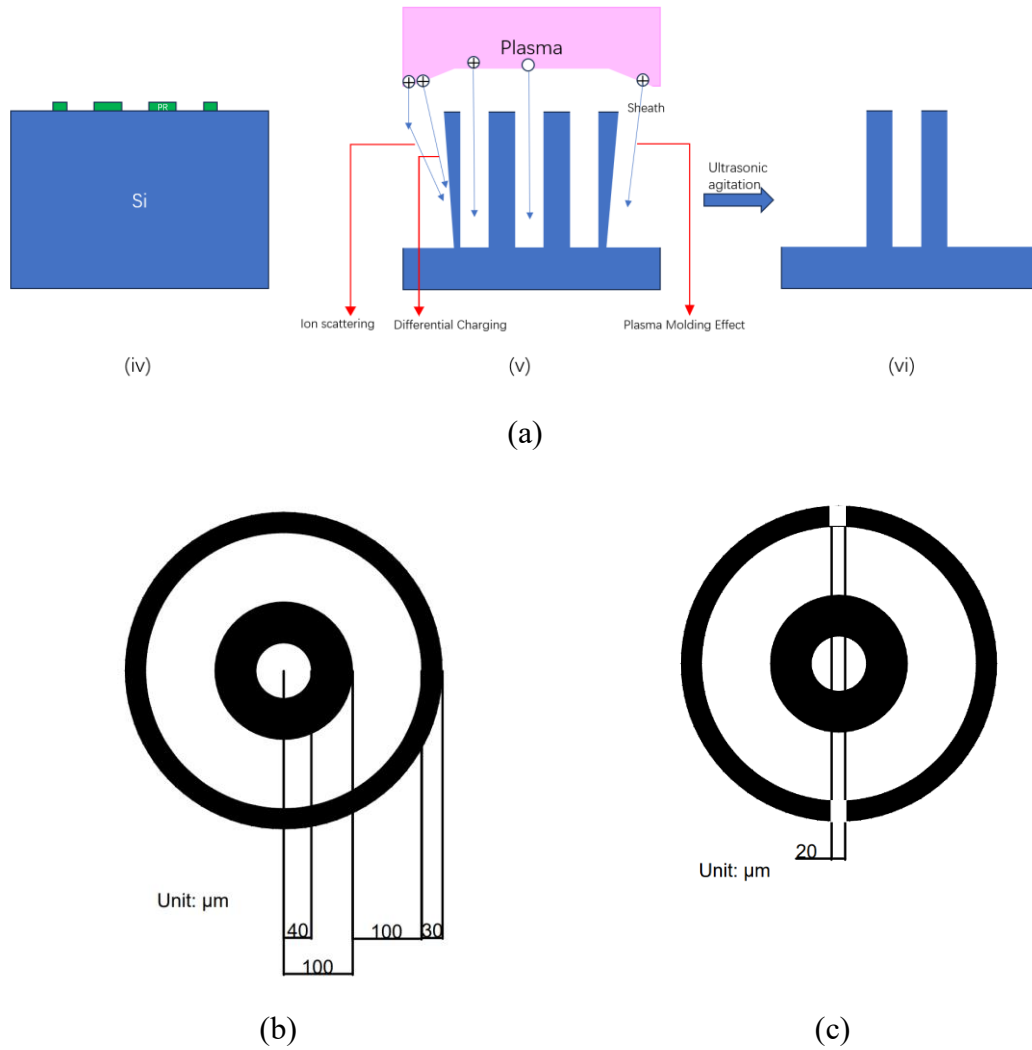


Figure 4.20 Design of the sacrificial structures. (a) sideview of the etching process with and without sacrificial structures; (i)-(iii) without sacrificial structures; (iv)-(vi) with sacrificial structures; (b) one full circle structure; (c) two half-circle structure, other dimensions in (c) are same as (b), the shadowed parts are covered by etch mask.

In our experiment, the anisotropic etching of the silicon pillars was conducted in an inductively coupled plasma reactive ion etcher (ICP-RIE). Specifically, the pillars were fabricated by Bosch DRIE recipe using Oxford Instruments PlasmaLab System100 etcher. The parameters of Bosch Process are listed in Table 4.7. In order to have a stable process in practice, we divide passivation step into two parts with different parameters. This DRIE system is configured for 4-inch wafers. To maintain wafer temperature at the constant value (15°C), the wafer was clamped with continuous helium backside

cooling during the process.

The patterns of pillars and sacrificial structures were fabricated using standard lithography. First, a 4-inch (100) p-type boron doped 1-30 Ωcm 1mm thick silicon wafer was cleaned by immersion into acetone, followed by isopropyl alcohol (IPA) rinsing, nitrogen blow drying, and oxygen plasma cleaning. Then, a layer of HTF-4025G negative photoresist (Hantop, China) was spun onto one side of the wafer with the thickness of $\sim 27\text{ }\mu\text{m}$. Next, ultraviolet (UV) direct write was carried out using a maskless aligner (MLA, Heidelberg DWL66+). The 405 nm laser power was 260 mW, and the strip length is 300 μm . Afterwards, development was performed by immersing the exposed sample into the developer solution (2.38% TMAH plus additives) for 5 minutes. The photolithography process formed an array of rings and the sacrificial structures around them. Figure 4.21 shows the microscopy image of the sacrificial structure patterns after photolithography. Later, DRIE (Bosch Process) was utilized to fabricate the high aspect ratio ring pillars with ideally vertical sidewalls. After etching process, the profile and parameters of the etched pillars were observed by scanning electron microscope (SEM).

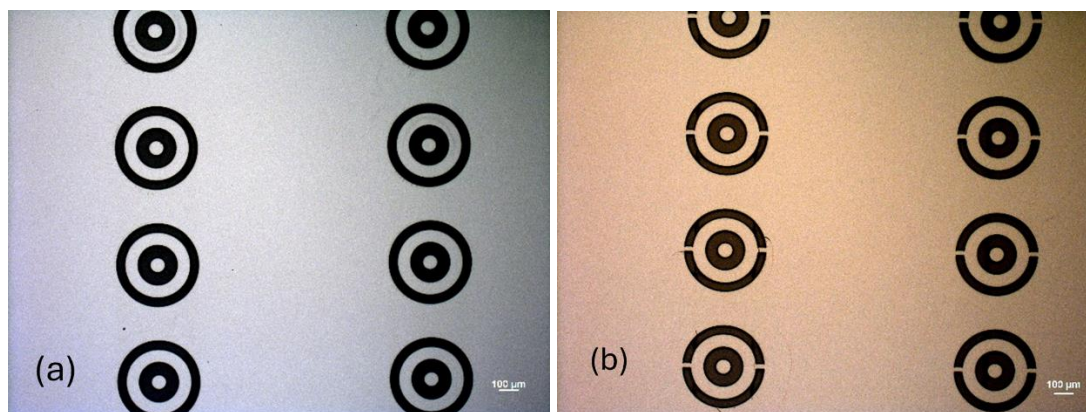


Figure 4.21 Microscopy images of ring pillar and sacrificial structure patterns after photolithography. (a) one full circle structure; (b) two half-circle structure.

Table 4.10 Parameters of the DRIE etching process (Bosch Process) with an RF frequency of 13.56 MHz at 15 $^{\circ}\text{C}$.

	Passivation 1	Passivation 2	Etching
ICP Power	900 W	700 W	1000 W
Cycle	2 s	3 s	6 s
Gas	C ₄ F ₈	C ₄ F ₈	SF ₆
Flow rate	100 sccm	100 sccm	100 sccm
RF Bias Power	15 W	6 W	15 W
Pressure	30 mTorr	30 mTorr	40 mTorr
Etch rate	0.25 $\mu\text{m}/\text{cycle}$, 1.4 $\mu\text{m}/\text{min}$		

4.5.1.3 Ring pillar etching test with sacrificial structures

The pillars were etched on a 4-inch Si wafer using Bosch Process with the parameters listed in Table 4.10. As shown in Figure 4.22, the etched pillars with no sacrificial structures are 397 μm high after 1600 cycles of Bosch Process. The outer diameter of the pillar was measured 200 μm at the top, same as the designed diameter. However, the diameter decreased to 96 μm at the bottom of the pillar, creating a reentrant profile; the sidewall angle is 62.5° with respect to horizontal level, showing great lateral etching at the bottom during Bosch Process.



Figure 4.22 Pillar structures etched without sacrificial structures.

For the pillars with one single circle sacrificial structures, Bosch Process was carried out for 1800 cycles. After that, SEM images were captured to observe the condition of sacrificial structures. Figure 4.23(a) shows the top view of the etched sample. Most of the sacrificial structures still remained on the sample. However, after 5 min of ultrasonic agitation in DI water, the remaining sacrificial structures were easily removed (Figure 4.23(b)). With the help of ultrasonic agitation, the design of the sacrificial structures would be easier since it would not be necessary to calculate the size of the sacrificial structures accurately. 470 μm high pillars were etched with nearly vertical sidewalls (sidewall angle 89.2°). The narrowest part of the pillar is 185 μm, compared to 197 μm at the top of the pillar, showing negligible lateral etching (Figure 4.23(c)). It can also be observed that there is a wider part at the base of the pillar, and this is caused by the ARDE effect inside the narrow gap between sacrificial structure and ring pillar. Also,

once the sacrificial structures are degraded during Bosch process, lateral etching will happen quickly, as shown in Figure 4.23(d): only $\sim 20\text{ }\mu\text{m}$ additional etching will reduce the sidewall angle from 89.2° to 87.1° .

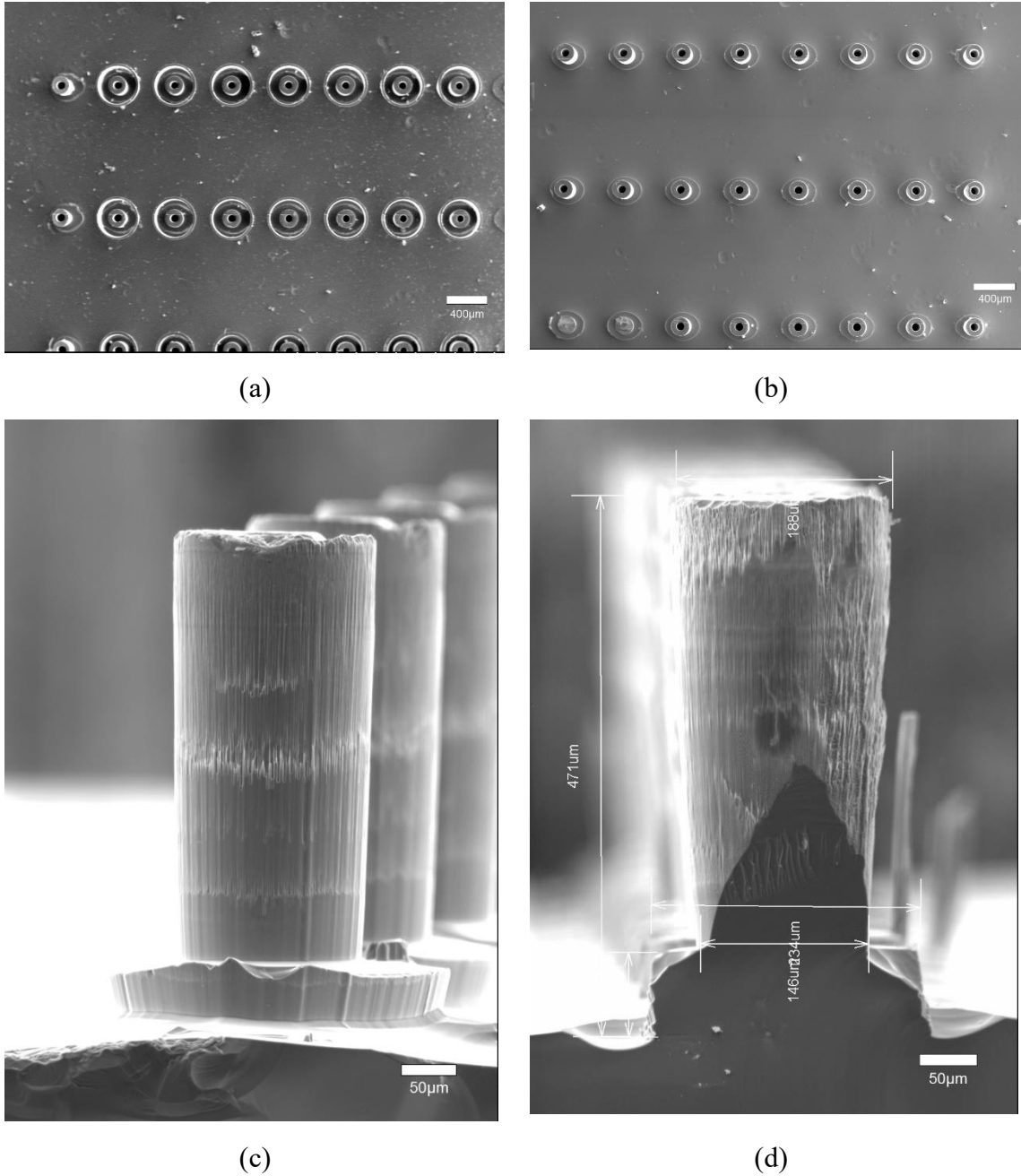
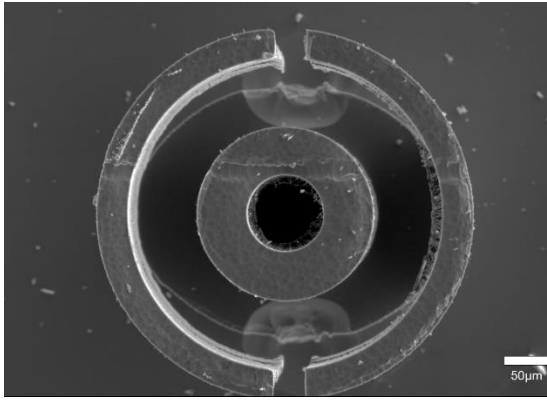


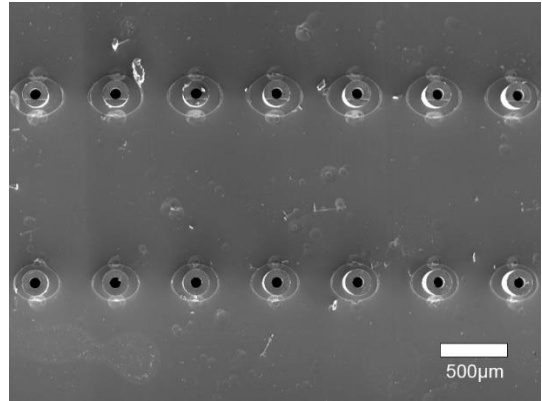
Figure 4.23 Silicon pillars etched with circular sacrificial structures. (a) Top view of pillars with circular sacrificial structures; (b) Top view of pillars with broken off circular sacrificial structures after ultrasonic agitation; (c) Sideview of pillars with circular sacrificial structures after ultrasonic agitation; (d) Side view of pillars with sacrificial structures collapsed before the end of etching, without ultrasonic agitation.

For the pillars with two-half-circle shape sacrificial structures, Bosch Process was carried out for 1800 cycles to etch 470 μm -high pillars with vertical and smooth sidewalls. After 1600 cycles, the sacrificial structures remained on the sample (Figure 4.24(a)); however, different from the one full circle structures, the sacrificial structures were almost totally removed by extending Bosch Process to 1800 cycles (Figure 4.24(b)), indicating that the degradation of two half-circle structure is faster than one full circle structure. This is probably because that the two gaps may slightly accelerate the lateral etching of the sacrificial structures since the free radicals like F can diffuse into the area between the pillar and the sacrificial structures via the gaps. For the remaining sacrificial structures, as shown in Figure 4.24(c), it is obvious that the degradation of the sacrificial structures occurs first near the gaps between the two half circles. With continuous etching process, the bottom part of sacrificial structures thins down faster. Once the bottom part of the sacrificial structures is too thin to support the half circle, the structures would break down. The extra degradation at the two gaps indicated that two-half-circle structures would degrade faster than one full circle structure. The pillar outer diameter is 198 μm and the inner diameter is 84 μm with negligible deviation from the designed 200 μm and 80 μm respectively. The narrowest part of the pillar is 193 μm , showing that the sidewall angle is 89.7° with respect to the horizontal level (Figure 4.24(d)). Figure 4.24(e) shows that the etching local uniformity was also good, as the pillars had almost the same height and sidewall profiles. Moreover, the surface was still clean with no grass formation. As a conclusion, both one sacrificial circle structure and two half circle structure can reduce lateral etching, which is crucial for etching high aspect ratio hollow pillars.

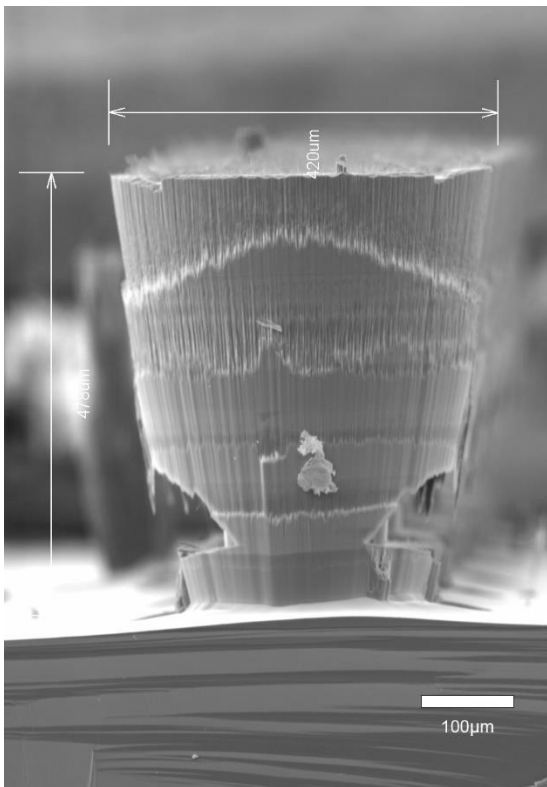
For the hole etching at the center of the pillar, as shown in Figure 4.24(f), the hole diameter is 83 μm , compared to the 84 μm diameter at the top, indicating nearly vertical sidewalls. The bottom of the hole remained flat; and the depth of the hole is about 370 μm , less than the 470 μm pillar height, caused by the ARDE effect.



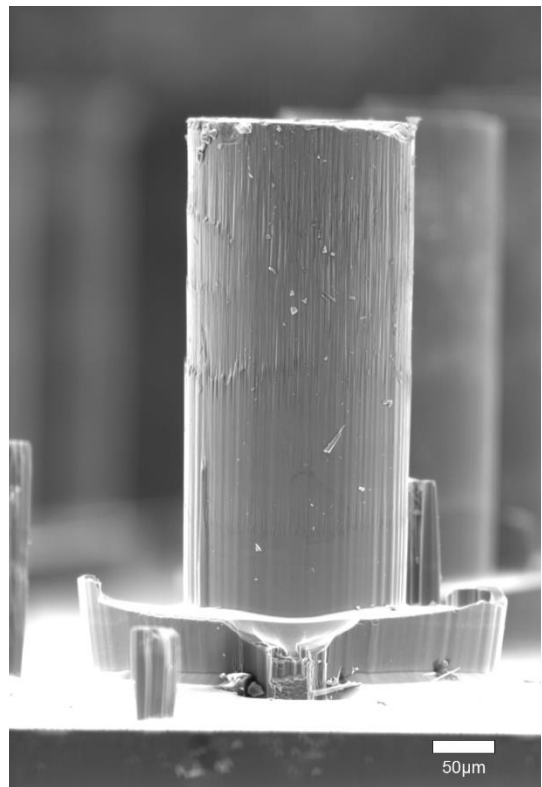
(a)



(b)



(c)



(d)

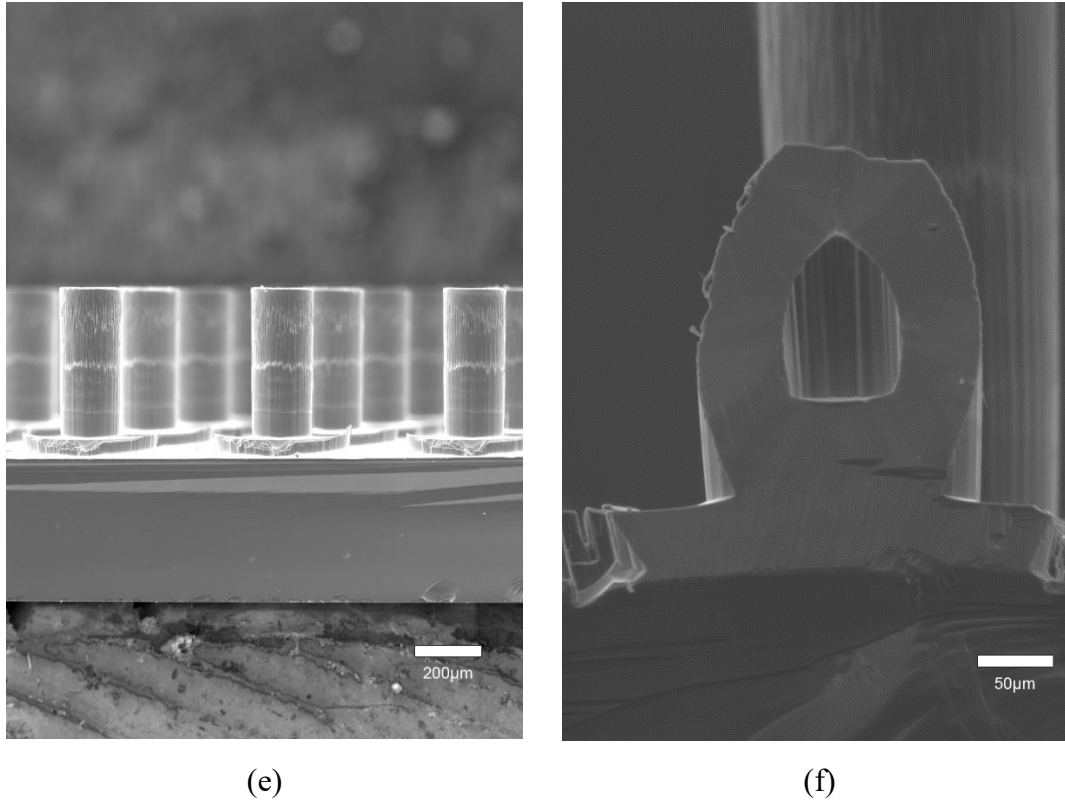


Figure 4.24 The hollow silicon pillars etched with two half-circle sacrificial structures. (a) Top view of pillars with sacrificial structures after 1600 cycles of Bosch process; (b) Top view of pillars after 1800 cycles of Bosch process; (c) Sideview of a pillar with sacrificial structures after 1600 cycles of Bosch process; (d) Sideview of a pillar after 1800 cycles of Bosch process; (e) Sideview of pillars, showing the etching local uniformity; (f) Sideview of hole structures at the center of pillars.

All in all, high aspect ratio ring (i.e. hollow) pillar array with good local uniformity is fabricated by using the Bosch process deep RIE with the help of sacrificial structures. Without the sacrificial structure, the etched pillars were greatly negatively tapered with a profile angle of 62.5 degree. With the sacrificial structure, we achieved etched pillar of 470 μm height and 200 μm outer diameter with nearly vertical (> 89 degree) sidewall; and for the hole at the center of the pillar, the diameter was 80 μm and the depth was 370 μm. We designed two kinds of sacrificial structures, namely full circle and two half-circle with a gap in-between, and demonstrated that both sacrificial structures can effectively reduce lateral etching during Bosch Process to ensure a vertical sidewall. In

addition, the sacrificial structures could be easily removed after the etching process using ultrasonic agitation, making the process practical for the fabrication of hollow microneedles.

4.6 Completed silicon hollow microneedles

After frontside ring pillar etching, the sample was processed using oxygen plasma to remove the remaining fluorocarbon polymer. Then, RCA-1 cleaning was performed, and the fabrication steps are completed. Figure 4.25 shows the chip of the microneedle arrays, and we can see the beveled tips and holes with good uniformity. Additionally, we used SEM to observe our microneedle structures.



Figure 4.25 Completed microneedle chip.

As shown in Figure 4.26, 600 μm high pillars with 54.7° slope were etched after 1000 cycles of Bosch process by Samco RIE-iPB800, forming the final schematics of microneedles. The narrowest part of the pillar was 189 μm and the sidewall angle was 86.9° . The microneedle tips were observed to be sharp, and the chip exhibited good uniformity, indicating the stability and reliability of the fabrication process.

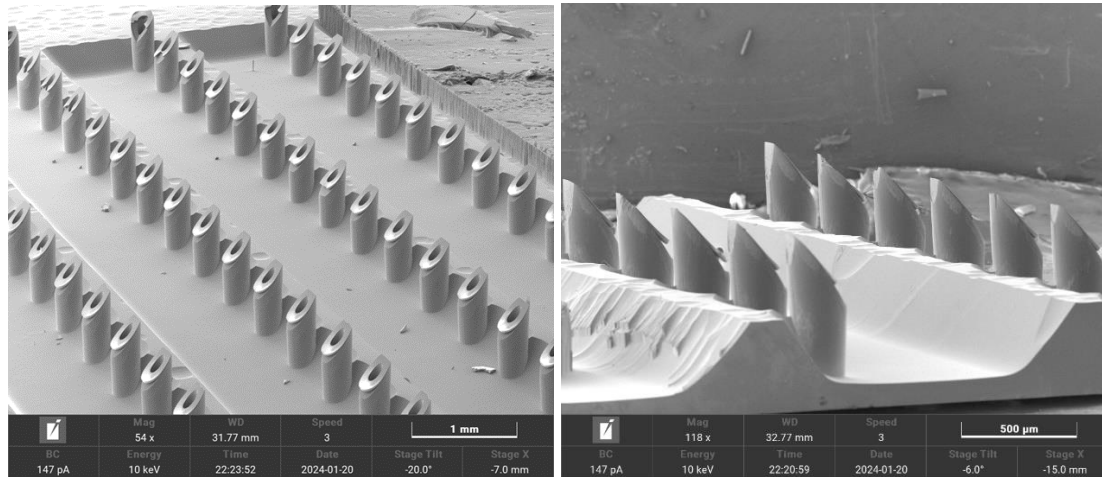


Figure 4.26 SEM images of microneedles with 54.7° slope.

For microneedles with 45° slope, the pillars were etched after 1000 cycles of Bosch process using Oxford Estrelas 100 etcher in nanoFAB, University of Alberta. As shown in Figure 4.27, 600 μm microneedles were successfully fabricated. The narrowest part was 164 μm, forming 79.8° sidewall. The tips are sharp and the uniformity of the chip was good.

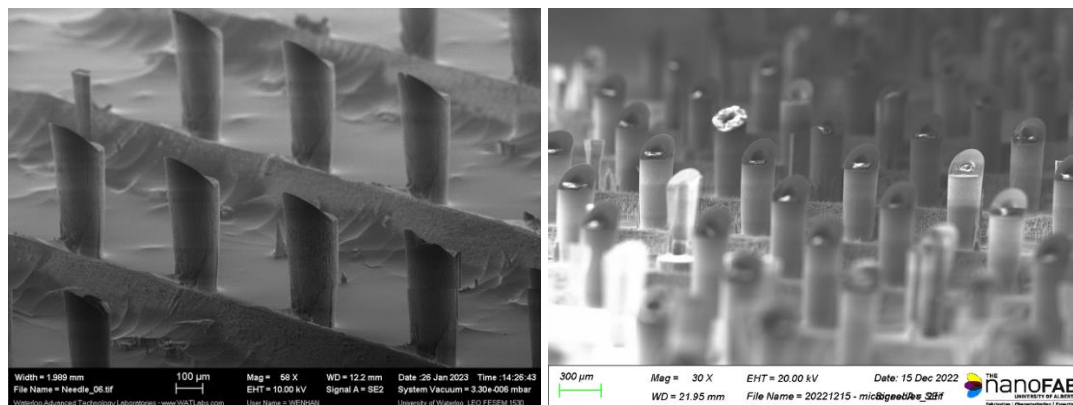


Figure 4.27 SEM images of microneedles with 45° slope.

Compared to our microneedle and the microneedle produced by NanoPass (Figure 1.17), which is also a beveled tip microneedle. The proposed method has several superiorities. First, we can fabricate microneedles with higher aspect ratio, since in our method, the aspect ratio is mainly determined by Bosch process. The aspect ratio can be increased by increasing the time of Bosch process. On the contrary, the aspect ratio of NanoPass

microneedle is limited by KOH wet etching. The aspect ratio is fixed at 1.41 ($\tan 54.7^\circ$), since the slope is fixed as the (111) plane, while we can achieve an aspect ratio of 3 for the outside pillar. Furthermore, the ability to fabricate microneedles with higher aspect ratios means that, for a given height of 600 μm , the base area of our microneedle is 0.031 mm^2 compared to 0.085 mm^2 for the NanoPass microneedle. Consequently, during the drug delivery process, our microneedle will inflict 64% less damage to the skin area than the NanoPass microneedle, highlighting its minimally invasive property. Additionally, the reduced contact area of our microneedle allows for the application of less force to penetrate the skin, as higher pressure can be achieved, thereby reducing the risk of leakage. However, the small hill remained beside the pillars is the drawback of our microneedles.

4.7 Test of the microneedles

Since the fabrication process was completed, it was necessary to test the various functions of fabricated microneedles. First, the sample was cut into small pieces with of $\sim 3 \text{ mm} \times 1.5 \text{ mm}$. We then stick the sample piece onto the polymer applicator fabricated by 3D printing (Figure 4.28(a)) using glue. The tapered cone shape applicator has a circular base with 4 mm diameter while there is a 2.3 mm x 0.9 mm notch at the top. For the sample piece, there were ~ 3 microneedles on the chip. However, since the notch area is smaller than the chip size and the presence of glue, there were only two needles on the chip connected to the barrel. The applicator can connect the syringe and the sample piece, as shown in Figure 4.28(b), replacing the traditional hypodermic needle.



Figure 4.28 Microneedle test device manufacturing. (a) Polymer applicator fabricated by 3D printing; (b) Microneedle chip connecting syringe with applicator.

4.7.1 Extraction test

In this test, we used the syringe to extract diluted blue ink. As shown in Figure 4.29, we first immersed the microneedle part into the ink in the petri dish. Subsequently, the plunger of the syringe was pulled, drawing the blue ink into the barrel and demonstrating the successful extraction function of the microneedle. It was noted that some air was also extracted. This is because we only immersed the needle part into the ink, which was very thin, and we could not hold our hands at a stable position, so the needle tips were exposed to air for some time. This issue can be mitigated by ensuring the microneedle tip is deeply immersed in the ink.

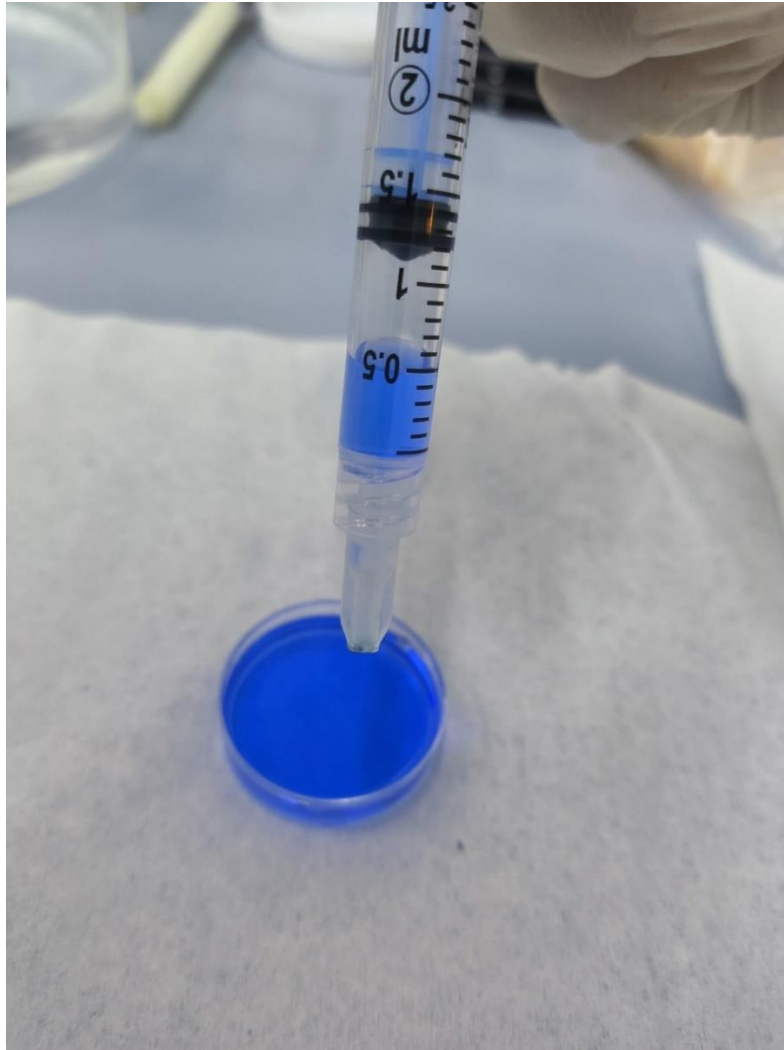


Figure 4.29 Capillary filling and microneedle extraction of blue ink.

4.7.2 Injection test

Next, we tested whether the liquid could be released from the needle barrel. We first extracted some water into the barrel and then put the syringe upward, as shown in Figure 4.30. Next, we gently pushed the plunger. We can observe two powerful water beams spurting out through the holes of the microneedle chip. This confirms that the hollow structure of our microneedles can function as a tunnel to transport liquid, showing that our microneedle chip can inject liquid in a manner similar to the traditional hypodermic needle.

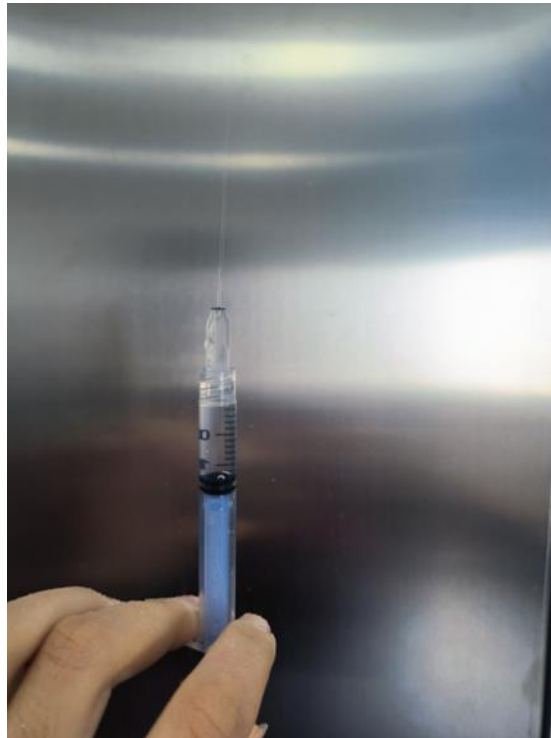


Figure 4.30 Water injection through microneedle.

4.7.3 Drug delivery test

Afterwards, the “drug” (here, blue ink, not actual drug) delivery test was assessed with excised porcine skin. Porcine skin is often used as a model for human skin due to the similarities in anatomy such as the thickness of the stratum corneum. The insertion force is suggested to range from 0.1 to 3 N, such that a regular thumb-push is sufficient for skin penetration, rather than requiring aid from impact-insertion applicators with elastic triggers to provide extra momentum. A razor was used to remove the subcutaneous fat on the back of the skin, making 1 cm-thick porcine skin samples. Then, the skin with good surface conditions (without hair or skin disorders such as scarring) was cut into rectangular piece for experimentation. As shown in Figure 4.31, we first extracted some blue ink into the barrel, then held the syringe and gently pushed the needle part into the porcine skin. Subsequently, we pushed the plunger to simulate the

drug delivery environment. The microneedles pierced the skin first and then transferred the blue ink through the holes. The penetration process is smooth without the addition of the force. We also tried to do the penetration process on different places of the porcine skin with the same microneedle piece, showing no difficulties, indicating that the microneedles are solid enough for repeated penetrations. Successful skin penetration is largely attributed to the extreme sharpness of the microneedles, as the insertion pressure linearly decreases with the interfacial area of the needle tip. Figure 4.32 shows the photo and microscopy image of the piercing points on porcine skin after drug delivery. The blue dots (circled part) caused by ink injected into the porcine skin indicate successful drug delivery.

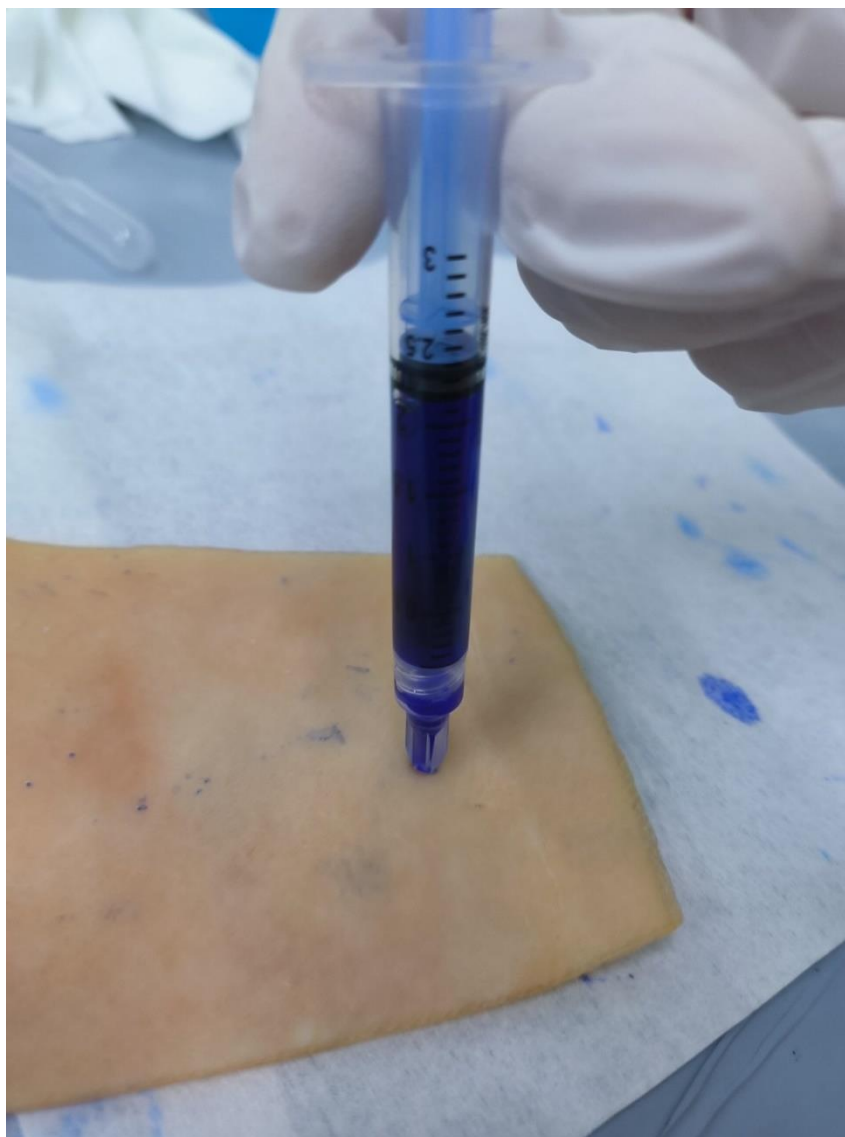


Figure 4.31 Microneedle penetrations into porcine skin.

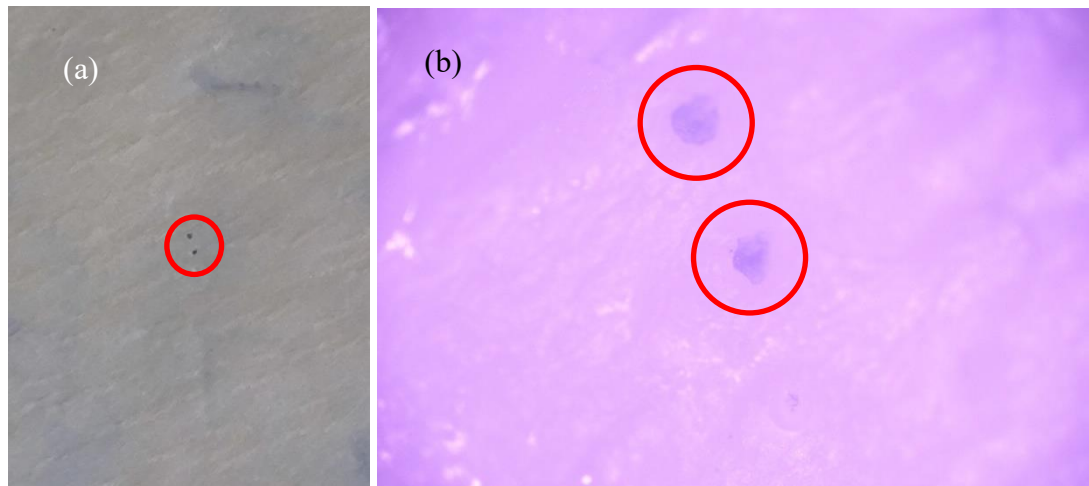


Figure 4.32 (a) Original and (b) microscopy image of the porcine skin after blue ink delivery.

4.7.4 Mechanical test

A mechanical test should be applied to evaluate the penetration ability and ensure that the microneedles will not collapse after injection.

We selected the Instron 5548 micro tester to evaluate the mechanical test. The Instron 5548 micro tester is capable of applying up to 1000 N static force. Considering that each microneedle's tolerance limit is less than 10 N, a 1000 N load cell is suitable. As shown in Figure 4.33, the microneedle chip was fixed on the platform under the vertically moving mechanical sensor. Then, the microneedle chip was compressed by the vertically moving sensor with a constant velocity of 0.5 mm/min. The displacements of the sensor and the forces applied on the microneedle chip were recorded by the computer when the bottom of the moving sensor touched the tip of the microneedles. The data were recorded every 0.05 s. The measurement would be stopped when the force increased linearly to ~400 N, which means all the microneedles had been broken, and the sensor was compressing the substrate of the microneedle chip. Figure 4.34 shows a microneedle chip after the mechanical test, and all the needles are collapsed

with only substrate remaining. After the test, the displacement-force curve was obtained accordingly.



Figure 4.33 Instron 5548 micro tester. The microneedle chip is placed on the platform (circled area).

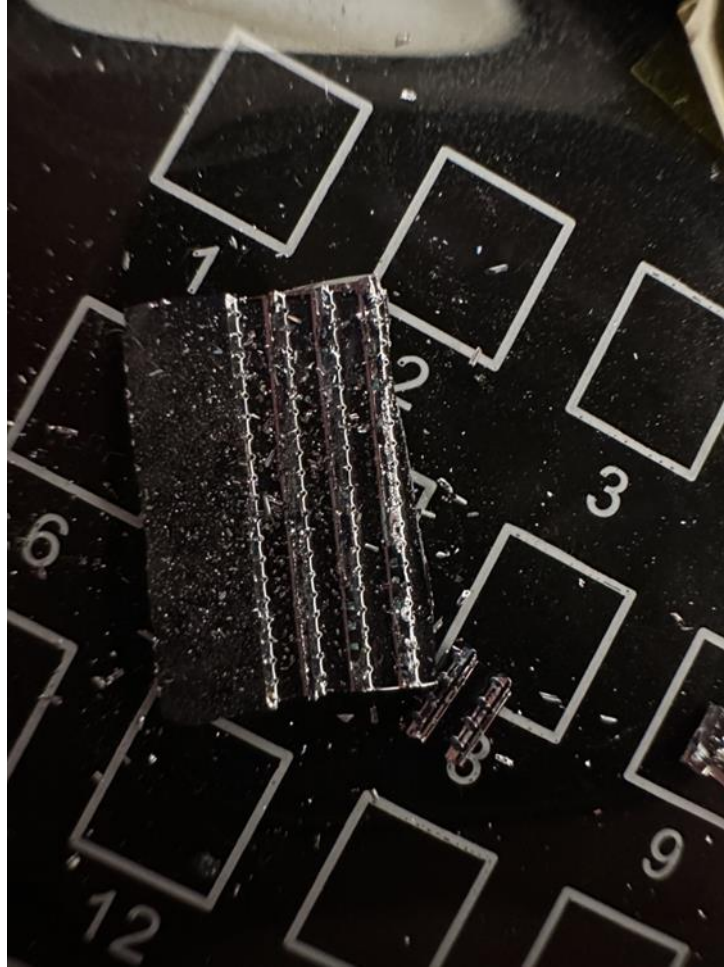


Figure 4.34 Microneedle chip after mechanical test with all the needles collapsed.

To test the maximum tolerance force accurately, we tested five samples. Sample 1 and sample 2 are relatively big samples with 80-100 needles on each sample. Sample 3, sample 4, and sample 5 are small samples with 4-10 needles on each sample. Figure 4.35 shows the force-displacement curve of sample 1. From the curve, we can see that the maximum force on the chip is 244.16 N, showing that the maximum force on each microneedle is approximately 3.05 N. Moreover, there is a sudden decrease right after the maximum point, which shows the characteristic of brittle fracture of the microneedles, according to the material property of silicon at room temperature. Similarly, we obtained the maximum tolerance force for sample 2, 3, 4, and 5 from the data recorded by the sensor. Then, we divided the force by the number of needles to obtain the maximum tolerance on a single needle.

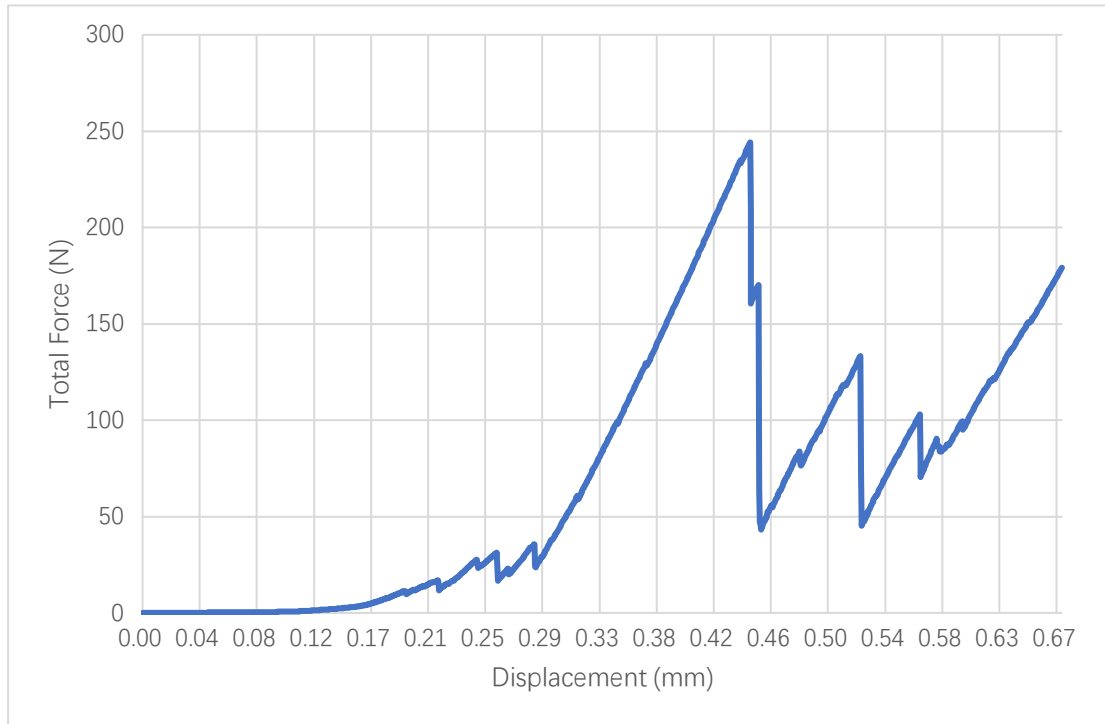


Figure 4.35 Force-displacement diagram for sample 1.

Table 4.11 summarizes the results of the maximum force for all 5 samples. It can be found that for big samples and small samples, the maximum average tolerance force on each needle is approximately 3 N.

Table 4.11 Max total force and max average force on each needle for all samples.

	Number of the microneedles	Max total force (N)	Max average force on each needle (N)
Sample 1	80	244.16	3.05
Sample 2	100	331.89	3.32
Sample 3	10	29.75	2.98
Sample 4	4	11.76	2.94
Sample 5	7	22.26	3.18

Typically, to penetrate the skin, the force should be at least 0.1-0.4 N^{126,127,128}. Since our microneedle can stand 3 N on each needle, which is much larger than the minimum

required force, it can be confirmed that our microneedle has great mechanical strength, and it can penetrate the skin safely without collapse. The outstanding mechanical strength is also an important reason for us to select silicon as the material.

In summary, we tested and confirmed the fundamental functions of our hollow microneedles for drug extraction, injection, drug delivery, and good mechanical strength, showing that our microneedles can potentially be used in practice.

Chapter 5

Fabrication of silicon out-of-plane hollow microneedles by DRIE and grayscale lithography

This chapter introduces an alternative method for fabricating silicon out-of-plane beveled tip microneedles, analogous to the process described in Chapter 4, employing grayscale lithography and DRIE. The chapter also presents the results obtained after each fabrication step, along with the optimization methods implemented to enhance the process.

5.1 Overall design of silicon out-of-plane microneedles with beveled sharp tip by grayscale lithography and DRIE

Grayscale lithography is used to produce 3D structures on micro and nano scale. During grayscale lithography, a variable-dose exposure is used to control the height of the developed photoresist, resulting in a 3D resist structure after development.^{129,130} Therefore, in this chapter, we propose another method to fabricate microneedles with the same shape as that in Chapter 4 by grayscale lithography. As shown in Figure 5.1, grayscale lithography can form resist structures with different heights. Using UV direct writing technology, we can easily achieve different doses in different locations on the wafer. In this way, when etching the pillars, the thinner photoresist would be etched away first, causing etching of the silicon underneath, and the sharp slope would be

fabricated by only one single step instead of several steps.

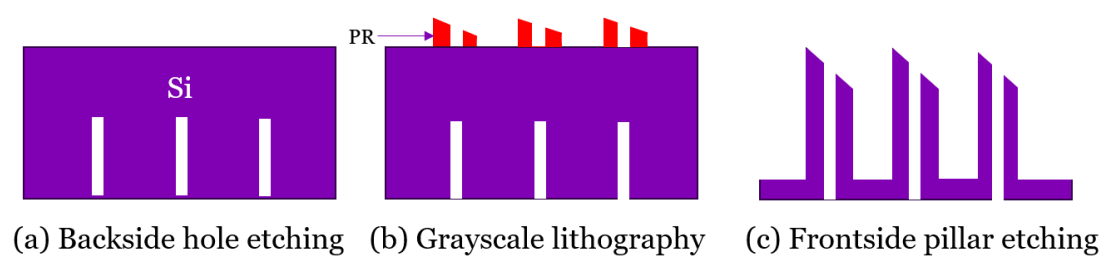


Figure 5.1 Process flow of microneedle fabrication based on grayscale lithography. (a) Backside hole etching; (b) Grayscale lithography to form slope-shape rings; (c) Frontside pillar etching.

5.2 Backside hole etching

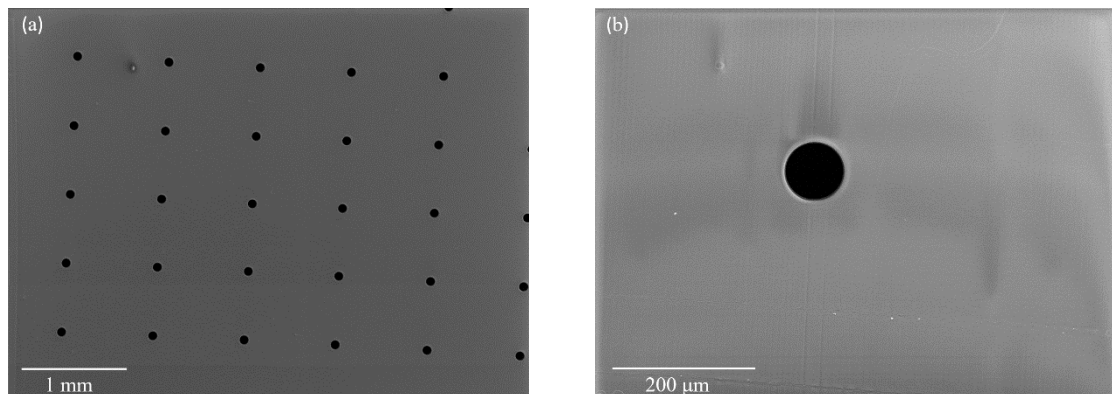
Initially, a 700μm thick (100) 4-inch double-side polished silicon wafer, which was pre-cleaned by rinsing in acetone and isopropanol, and then treated with oxygen plasma to further remove organic pollutants, was prepared. Then, a layer of 6.4 μm SUN-9i photoresist was spin-coated on the back of the silicon wafer at 1400 rpm and baked at 110°C for 90 seconds. After cooling, the resist was exposed in MLL-C900 UV direct writing maskless aligner with 405nm wavelength laser for 530mW. After exposure, post exposure bake was carried out on a hot plate at 110°C for 90 seconds, following the development in AZ 300 MIF for 2 minutes. The developed patterns were holes with 80 μm diameter, and then the silicon substrate was etched by Bosch process (the recipe is listed in Table 5.1) to a depth of ~400μm. After that, the remaining photoresist was removed in the stripping solution, and the sample was cleaned by rinsing in isopropanol.

Table 5.1 Parameters of the DRIE etching process on Samco RIE-iPB800 for backside hole etching (Bosch process) with an RF frequency of 13.56 MHz at -10 °C.

Passivation	Breakthrough	Etching
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ICP Power	4500 W	750 W	4500 W
Cycle	2 s	2.5 s	14 s
Gas	C ₄ F ₈	SF ₆	SF ₆
Flow rate	200 sccm	200 sccm	600 sccm
RF Bias Power	0 W	500 W	0 W
Pressure	15 mTorr	12 mTorr	38 mTorr
Etch rate	9.3 $\mu\text{m}/\text{cycle}$, 30 $\mu\text{m}/\text{min}$		

The total time of Bosch process lasted approximately 13 min, and the etch rate of silicon was approximately 30 $\mu\text{m}/\text{min}$. This optimized process allowed for a high selectivity of more than 150:1 between silicon and the photoresist in our experiment. Therefore, a thin layer of photoresist with 6.4 μm thick is sufficient as a mask to etch 400 μm deep holes in a 700 μm thick silicon substrate. As shown in Figure 5.2, holes with 80 μm diameter and 400 μm depth are well etched. From Figure 5.2, we can also observe that there are many scallop-shape profiles on the sidewall of the hole. This was because that the etching cycle is too long, and SF₆ isotropic etching contributed to the scallop-shape profile. To ensure a smooth sidewall profile, we can reduce the time of etching cycle at the expense of decreasing the etch rate. However, in this project, we didn't need a smooth sidewall, therefore we selected the fastest method.



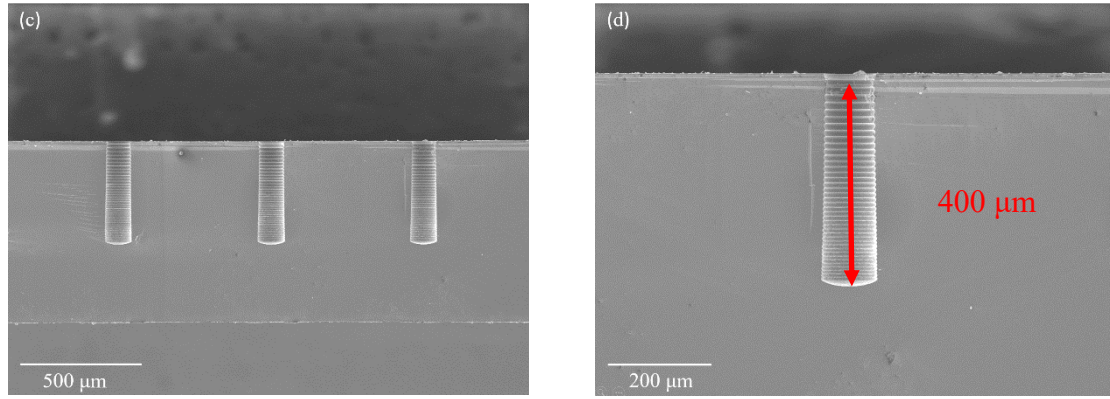


Figure 5.2 SEM image of through-holes with 400 μm deep and a diameter of 80 μm . (a) Top view of holes array; (b) Top view close-up image; (c) Cross-sectional image of the hole; (d) Cross-sectional close-up image.

5.3 Grayscale lithography

5.3.1 Contrast curve measurement

Before conducting grayscale exposure, it was necessary to test the sensitivity of the photoresist to different exposure intensities, which was mainly reflected in the residual thickness of the photoresist developed under different exposure intensities. We chose SUN-9i photoresist, which is a negative photoresist. We first prepared a resist film with a thickness of 6.4 μm (1400 rpm, 700 rpm/s² for 40 s) and pre-baked it on a hot plate at 110°C for 90 seconds before exposure. Then, we exposed different areas from 10 mW to 205 mW with 5 mW laser power as the step. Since we used MLA, we can only obtain the laser power rather than the exposure dose, so we can only get the relationship between the remaining resist thickness and laser power. After exposure, the resist was developed in AZ 300 MIF. The target resist profile is not straightforward to achieve, which is not only related to the complex nonlinear interaction between the resist and light, but also influenced by chemical development. In particular, a slight change in the

final development temperature and time affected the final photoresist structure profile¹³¹. In this way, to obtain the contrast curve accurately, we fixed the development time at 2 min 45 s and the temperature at room temperature. The residual photoresist thickness after development is measured using a profilometer (Dektak). The contrast curve between the remaining thickness of the photoresist and the exposure intensity is shown in Figure 5.3.

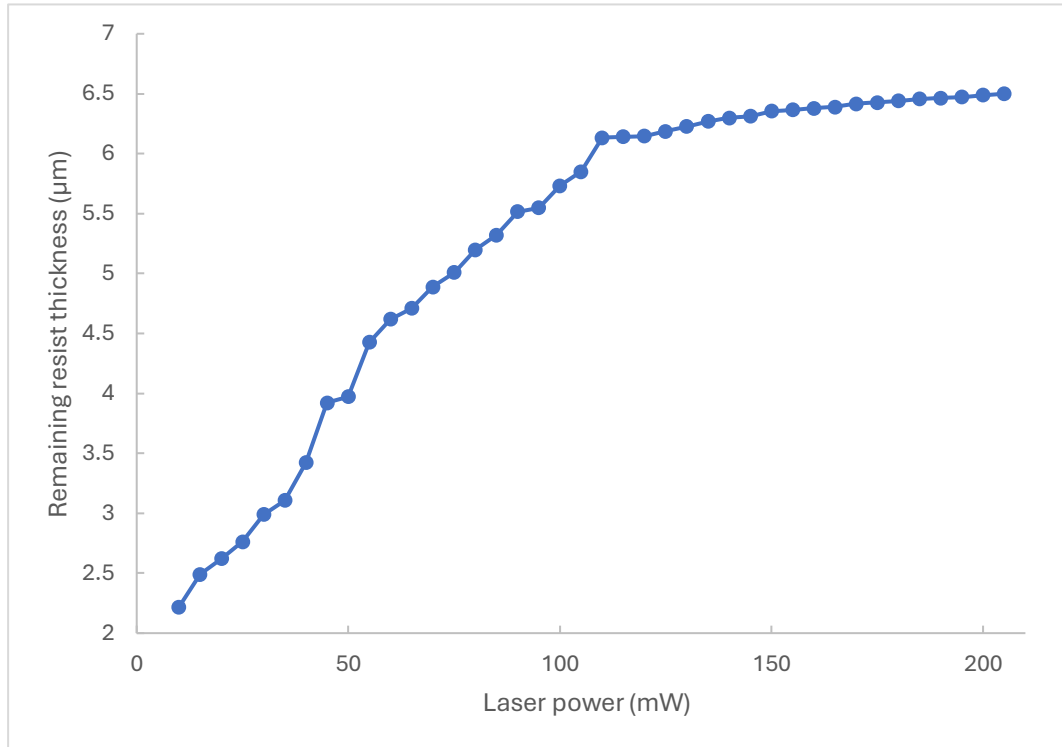


Figure 5.3 Contrast curve of remaining height of photoresist (SUN-9i) and laser power.

5.3.2 Frontside patterning by grayscale lithography

For the fabrication of photoresist structure, we used the contrast curve above to obtain the energy required for the corresponding gray exposure. Initially, a layer of HMDS was coated using an HMDS oven at 130°C to improve adhesion. A layer of SUN-9i photoresist was spin-coated with the same parameters as in the previous backside process. In the case of gray-scale exposure, considering the required 3D photoresist

profile, the mask must be designed into multiple layers. As shown in Figure 5.4, the mask pattern is a ring shape in which different colors represent different layers. Ideally, the resist should form a smooth profile representing infinite number of layers, which is not realistic. Thus, we can only form stepped profile. For the number of the layers, if it is too low, the top slope would be too rough, while if the number of the layers is too high, the entire process would be time-consuming since the lithography is completed layer by layer. In order to balance the slope profile and process time, we chose to divide the ring into 10 layers for gray-scale exposure, and each layer was assigned a specific exposure energy during exposure. The outer diameter of the ring was 200 μm and the width of each layer was 20 μm . The exposure energy of each layer was selected according to the requirements of the photoresist profile through the contrast curve in Figure 5.3, and the ten layers were assigned different exposure energies. At the same time, backside alignment needs to be applied since we need to align the hole on the frontside with the etched hole on the backside.

The specific laser powers and resist thicknesses for each layer from left to right in Figure 5.4 are listed in Table 5.2. Specially, the photoresist thickness doesn't increase linearly. Subsequently, the sample was developed in AZ 300 MIF under the same conditions as those used for testing the contrast curve. The photoresist profile can be optimized by slightly changing the exposure energy of the sudden depth transition around it. The scanning electron microscope image of the ring after gray exposure and development is shown in Figure 5.5. The ring-shaped photoresist structure has an inner diameter of 80 μm and an outer diameter of 200 μm .

Table 5.2 Exposure power of each layer in grayscale photolithography.

Layer	Laser power (mW)	Photoresist height(μm)
1	45	3.01
2	50	3.66
3	55	3.85
4	60	4.43
5	65	5.19
6	75	5.43
7	85	5.79

8	98	6.02
9	110	6.22
10	130	6.41

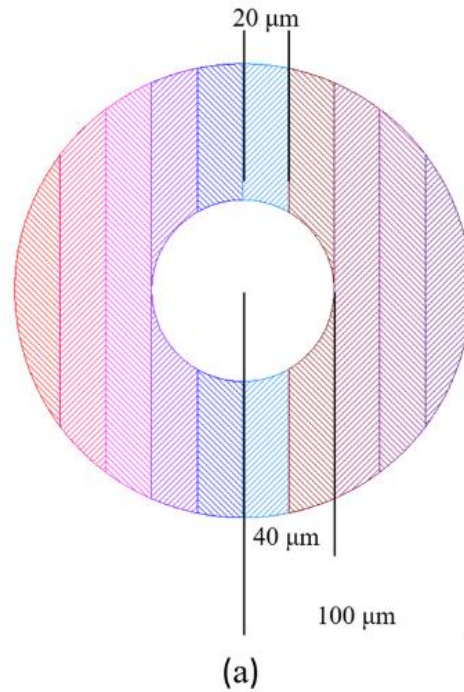


Figure 5.4 Pattern design of gray-scale lithography mask and outline after exposure and development.

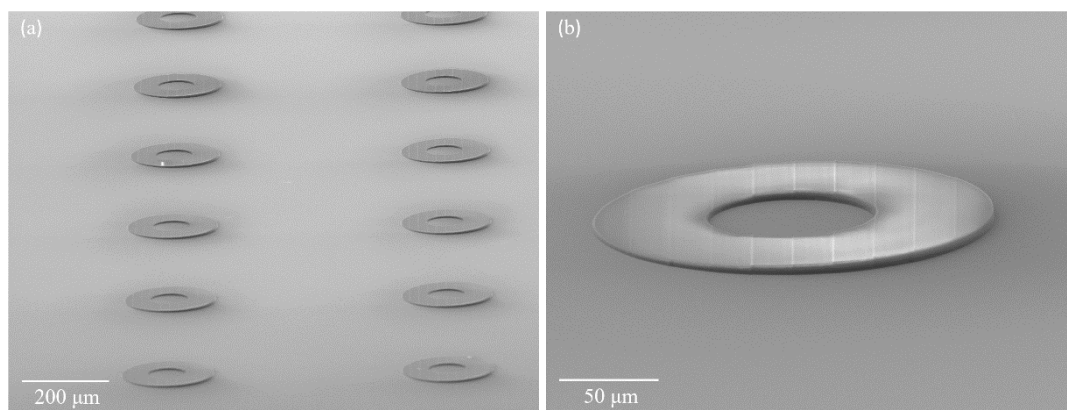


Figure 5.5 SEM image of ring structure obtained by grayscale lithography. The inner diameter of the ring is 80 μm and the outer diameter is 200 μm . (a) Top view of photoresist profile; (b) Top view close-up image.

5.4 Frontside pillar etching

Frontside pillar etching was achieved using DRIE to transfer the grayscale resist pattern into silicon. In this project, the etching was completed on Samco RIE-iPB800 RIE, and the recipe is listed in Table 5.3. Compared with the recipe used to etch holes, there are some differences. First, we increased the breakthrough time from 2.5 s to 4 s. The main purpose for this adjustment is to reduce the selectivity between the silicon and photoresist. The selectivity should be well controlled, since the profile of the silicon bevel is determined by its selectivity. The height difference between the two steps on silicon slope can be calculated by multiplying the selectivity and the height difference of the thickness of the resist in two layers. In this project, we expect a 200- μm high slope, so that the selectivity should be around 60, and we can obtain a 360- μm high pillar. Using this method, the selectivity was successfully decreased from 150 to 57. As the main factor in photoresist mask etching is physical sputtering, and ion bombardment mainly occurs in the breakthrough step, we need to slightly increase the passivation layer to increase fluorocarbon polymer deposition on the sidewalls since ion bombardment can also remove the fluorocarbon polymer protection layer, causing a reentrant profile.

Table 5.3 Parameters of the DRIE etching process on Samco RIE-iPB800 for frontside pillar etching (Bosch process) with an RF frequency of 13.56 MHz at -10 °C.

	Passivation	Breakthrough	Etching
ICP Power	4500 W	750 W	4500 W
Cycle	2.5 s	4 s	14 s
Gas	C ₄ F ₈	SF ₆	SF ₆
Flow rate	200 sccm	200 sccm	600 sccm
RF Bias Power	0 W	500 W	0 W
Pressure	10 Pa	1.6 Pa	30 Pa
Etch rate	3.1 $\mu\text{m}/\text{cycle}$, 9 $\mu\text{m}/\text{min}$		

Figure 5.6 illustrates the etching results after 40 minutes. The pillar height was 336 μm , with the photoresist mask's thickest part just etched away. The pillar's widest section measured 184 μm , showing some erosion of the photoresist, while the narrowest section was 170 μm , indicating an 87° sidewall inclination angle. The slope exhibited a stepped profile with a height of approximately 162 μm , corresponding to a 41° slope.

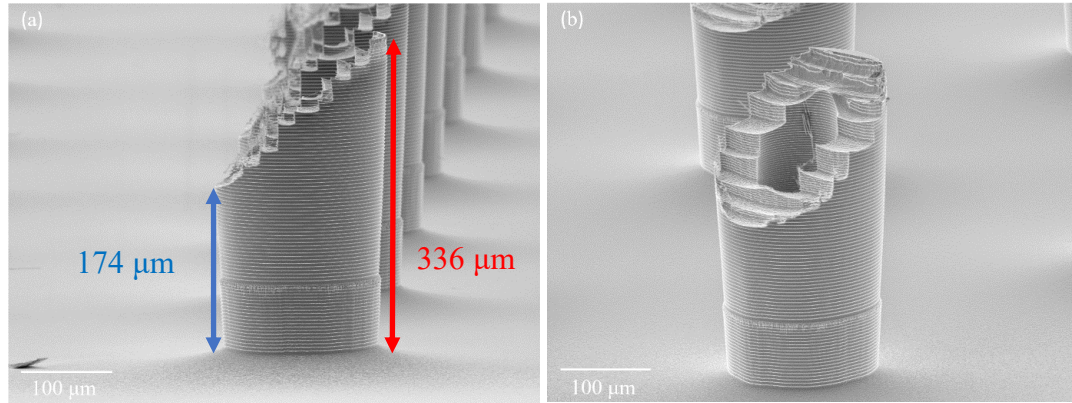


Figure 5.6 SEM image of etching results of microneedles after Bosch process.

At this time, the needle tip is composed of multiple steps, which may affect the penetration of the microneedles. We attempted to optimize the tip by isotropic etching of SF_6 to reduce roughness. Here, we chose to further etch the sample shown in Figure 5.6 with pure SF_6 to obtain a smoother needle tip profile. The process parameters for SF_6 etching are listed in Table 5.4. The sample was etched for 2 minutes using this recipe, and the result after etching are shown in Figure 5.7. Compared to the step profile in Figure 5.6, the shape of the needle tip gradually became smooth due to the isotropic etching of SF_6 , and the step profile was more naturally continuous. As for the results after SF_6 etching, we found that some steps could not be smoothly connected (red circled area), because the gradient difference between the two photoresist layers produced at the beginning of grayscale lithography is relatively large, which was further enlarged in the subsequent DRIE process, leading to a situation in SF_6 etching could not fully smooth out them. One drawback of SF_6 etching is that, due to the isotropy of the etching, the sidewall is thinned with the enlargement of the hole inside at the same time. Moreover, the base silicon would also be etched, showing an isotropic profile at

the base of the needle (green-circled area), which may etch through the sidewall, causing leakage or collapse. The height of the pillar changed to 325 μm after SF_6 etching, and the slope height changed to 128 μm . While the diameter of the pillar reduces to 145 μm due to isotropic etching, the slope angle increases to 48.6°.

Table 5.4 Parameters of SF_6 etching process on Samco RIE-iPB800.

Parameter	Value
Step duration	2 min
Pressure	10 Pa
ICP power	3500 W
RF bias power	100 W
SF_6 flow	900 sccm
Etch rate of Si	10 $\mu\text{m}/\text{min}$

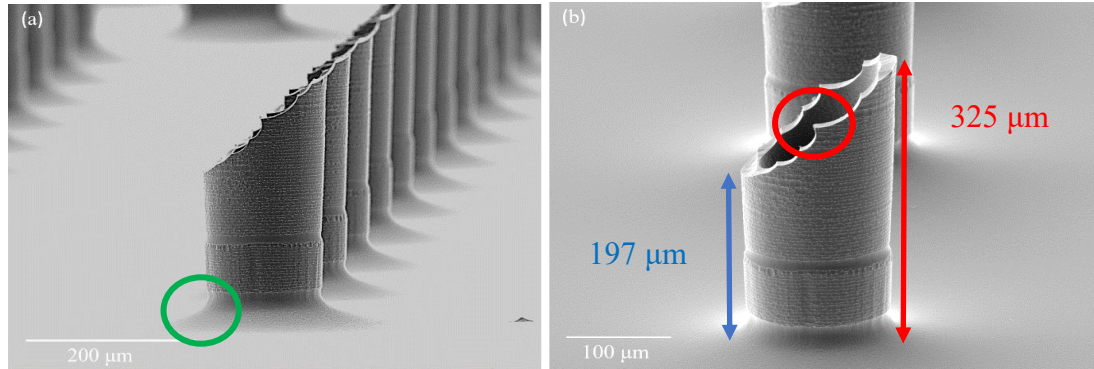


Figure 5.7 Morphology of microneedle optimized by SF_6 etching.

Another method to smoothen the beveled slope is to adjust the photoresist profile by thermal reflowing. Photoresist is sensitive to high temperature, which will be helpful for the fine adjustment of the photoresist structure after grayscale lithography, especially the gray structure obtained by low exposure energy^{132, 133}. When the photoresist was heated, the sharp corner was slightly rounded, leading to a smoother profile. We chose appropriate temperature (105 °C) and heating time (1 min) to conduct thermal reflow treatment on the photoresist obtained by gray-scale lithography before etching. The scanning electron microscope pattern of the photoresist structure after the

thermal reflow treatment and the profile scanned by the profiler are shown in Figure 5.8, showing a smooth slope profile of the photoresist.

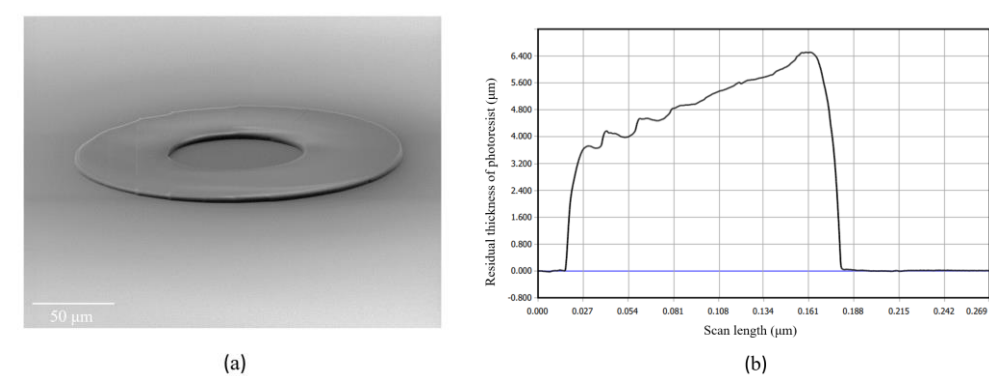


Figure 5.8 Photoresist mask structure after thermal reflow treatment. (a) Scanning electron microscope image of photoresist structure; (b) Photoresist profile after thermal reflow.

Subsequently, Bosch process was executed to etch the pillar. After Bosch process, 1 min SF₆ etching is carried out to remove the “glitch” (Figure 5.9 (a), circled area) created by fluorocarbon passivation layer during DRIE due to excessive passivation. The result is depicted in Figure 5.9 (b), showcasing a beveled tip microneedle with a height of 309 μm. The pillar width was measured at 163 μm, and the slope height was 47 μm, resulting in a 16° slope.

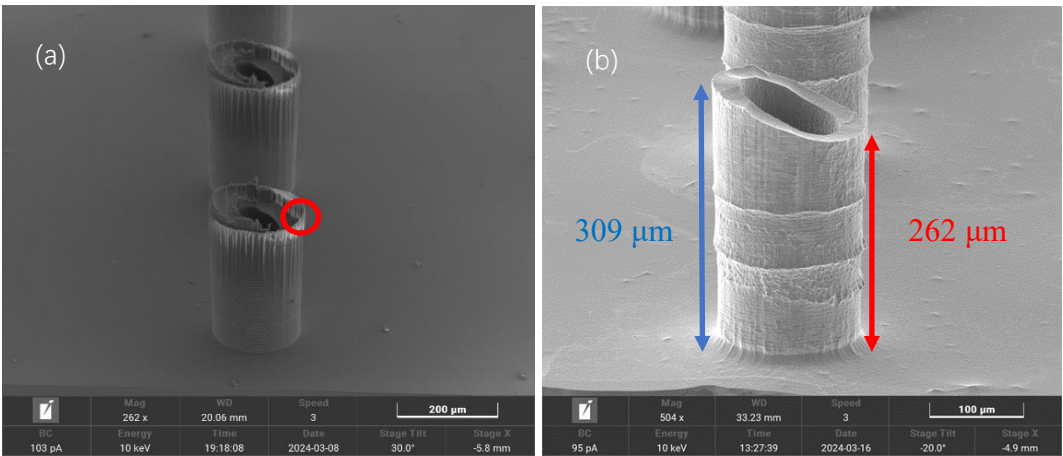


Figure 5.9 SEM image of microneedles after (a) Bosch process and (b) SF₆ etching subsequently.

In summary, microneedles were successfully fabricated using grayscale lithography and DRIE. Compared with the process flow described in Chapter 4, the slope etching is notably less complicated. Additionally, the flexibility in customizing the slope angle is enhanced since we can adjust the etching recipe for frontside pillar etching, allowing for great control over the etching selectivity between silicon and photoresist. However, a major drawback for this process is that grayscale lithography has poor reproducibility. We need to obtain the contrast curve every time we use grayscale lithography via MLA, which is time-consuming.

Chapter 6

Conclusion and future work

This chapter summarizes the achieved outcomes and the work we aim to complete in the future.

6.1 Comparison of our fabrication process with the work from prior art

Table 6.1 compares technologies of our microneedle fabrication process illustrated in Chapter 3, 4, and 5 with other work listed in Section 1.3.2, which are other fabrication methods for silicon out-of-plane microneedles. From the table, we know that the method developed by Roxhed et al. can fabricate microneedles with good parameters. However, it requires seven dry etching steps and the process is hard to control, complicating the process. Gardeniere et al. and O'Mahony et al. can form microneedles with more manageable steps. However, the aspect ratio is fixed to 1.41 for Gardeniere et al., since the exposed plane will be (111) plane. This will increase the base area of the needle, causing more damaged skin areas. For O'Mahony et al., the aspect ratio is also fixed since the exposed plane will be (311) plane. Moreover, the lateral etching during wet etching limits the needle density. For instance, the mask size has to be 3-5 times that of the target needle height. The fabrication process introduced in Chapter 3 can form cone-shaped microneedles with high needle density. However, it would be unlikely to fabricate microneedles longer than 300 μm due to the poor reproducibility and uniformity in the final wet etching step. It can be observed that for the process proposed in Chapter 4, the microneedles have the highest height, relatively large aspect ratio, and relatively small base area. The fabrication process requires relatively easy

etch steps and good reproducibility. Moreover, we can fabricate a beveled tip with a 45-degree slope or a 54.7-degree slope. Fabrication process introduced in Chapter 5 only needs two dry etching steps, which is the simplest one. Also, the flexibility of grayscale lithography enhances the possibility of customizing the slope angle. However, the worst reproducibility among these methods hinders this method for large-volume production.

Table 6.1 Comparison of parameters of microneedles fabricated by our fabrication process with the microneedle fabrication process by the work from prior art.

Method	Roxhed et al. ⁵⁶	Gardeniere et al. ⁶²	O'Mahony et al. ⁶⁴	Fabrication process in Chapter 3	Fabrication process in Chapter 4	Fabrication process in Chapter 5
Microneedle height	400 μm	600 μm	500 μm	160 μm	> 600 μm	~300 μm
Hole diameter	50 μm	100 μm	50 μm	30 μm	100 μm	100 μm
Aspect ratio (outside)	4	1.41	1.41	1.6	3	1.5
Aspect ratio (hole structure)	7	4.5	8	4	6	3
Microneedle density	4 needles/mm ²	1 needles/mm ²	0.25 needles/mm ²	11.1 needles/mm ²	1.2 needles/mm ²	2.8 needles/mm ²
Base Area (Damaged skin area)	0.0078 mm ²	0.085 mm ²	0.052 mm ²	0.0078 mm ²	0.031 mm ²	0.031 mm ²
Microneedle tip shape	Cone-shaped tip	Bevel tip	Cone-shaped tip	Cone-shaped tip	Bevel tip	Bevel tip

Etching steps required	7 dry etching steps	2 dry etching steps and 1 wet etching step	1 dry etching step and 1 wet etching step	2 dry etching steps and 1 wet etching step	2 dry etching steps and 1 wet etching step	2 dry etching steps
Reproducibility	Moderate	Good	Good	Moderate	Good	Poor

6.2 Conclusion and future work

Microneedle is one successful application of MEMS technology since it can form minimally invasive platforms to complete transdermal drug delivery, body fluid sampling and diagnosis, and silicon microneedles are desired due to their exceptional mechanical strength and biocompatibility. In this thesis, we focus on silicon microneedles fabrication using MEMS fabrication techniques.

We first fabricate silicon out-of-plane cone-shape hollow microneedles with sharp apexes and off-axis pores. Our process involves backside hole etching and frontside pillar etching via Bosch process, and pillar sharpening through HNO_3 -HF mixed solution. The sharpened microneedles are 160 μm high and the radius is 5 μm , enabling the penetration for drug delivery and in-vivo sampling of interstitial fluid. However, to penetrate the epidermis and access abundant body fluids in health monitoring systems, the needles should be higher and it is difficult to fabricate higher microneedles using this process due to the difficulties, especially inadequate uniformity in wet etching sharpening.

Then, we design a novel method to fabricate silicon out-of-plane hollow microneedles with beveled tip. The proposed method includes frontside slope etching, backside hole etching, and frontside pillar etching combining anisotropic wet etching and dry etching (Bosch process). The fabricated microneedles are ~ 600 μm high with beveled sharp tips. Moreover, the microneedle structure has high aspect ratio and low damage area to the skin compared to prior work. Furthermore, we test various fundamental functions of microneedles. We connect the chip with syringe with a 3D-printed applicator and successfully test the functions of liquid extraction, liquid injection, and simulate the drug delivery process. Also, we test the mechanical strength of the microneedles. The results show that each microneedle can tolerate 3 N force, indicating that the microneedles would not be broken after penetration.

During frontside pillar etching in the process flow, to minimize the influence on

inevitable lateral etching in Bosch process, we propose a novel structure, the sacrificial structure surrounding the pillars to shield the inside pillars from lateral etching. We test two types of sacrificial structures and both structures can effectively reduce the lateral etching, enabling the fabrication of 370 μm high ring pillars with vertical sidewalls, reducing the risk of collapse during pillar etching process.

Grayscale lithography combining subsequent Bosch process is another effective and flexible method to fabricate 3D structures like the bevel, so we can combine the frontside slope etching and frontside pillar etching in previous process flow into one step. In this way, we fabricate hollow microneedles measuring 325 μm in height. However, the poor reproducibility would be the barrier.

Since we've successfully fabricated the microneedles chips in lab, we're now pursuing the commercialization process. Considering the stability and cost, first, we change the form of deposition from PECVD SiN to thermal oxide. In this way, we can deposit SiO_2 on a large amount of wafers at the same time by thermal oxidation, which decreases the cost. Correspondingly, we change the wet etching method from KOH etching to TMAH etching. Another improvement is that we can try to fabricate on 6-inch or 8-inch wafers instead of 4-inch wafers, which is also advantageous for volume production.

Moreover, we can have more test on our microneedles. First, we can try our microneedles on animals to test drug delivery and body fluid extraction. Subsequently, we aim to integrate our microneedles on wearable devices for real-time health monitoring systems, thereby broadening the application of microneedles.

6.3 List of Publications

- W. Hu, Z. Wang, A. Pan, B. Cui, High aspect ratio silicon ring-shape micropillars fabricated by deep reactive ion etching with sacrificial structures, *Micro and Nano Engineering*, Vol. 22, 2024, 100234, ISSN 2590-0072. <https://doi.org/10.1016/j.mne.2023.100234>.

- W. Hu, Z. Wang, A. Pan, B. Cui, Fabrication of Sharp Silicon Out-of-Plane Hollow Microneedles with 45-Degree Bevel Tip Angle, Microneedle 2023 Conference.
- D. Zhang*, W. Hu*, B. Cui; Fabrication of hollow silicon microneedles using grayscale lithography and deep reactive ion etching. *J. Vac. Sci. Technol. B* 1 September 2024; 42 (5): 053001. <https://doi.org/10.1116/6.0003711>
- Y. He*, W. Hu*, B. Cui; Effect of Triton X-100 surfactant and agitation on tetramethylammonium hydroxide wet etching for microneedle fabrication. *J. Vac. Sci. Technol. B* 1 September 2024; 42 (5): 053001. <https://doi.org/10.1116/6.0003852>
- Y. Li, H. Zhang, W. Hu et al., Fabrication of Sharp Silicon Hollow Microneedles by Deep Reactive Ion Etching Towards Minimally-Invasive Diagnostics, *Nature Microsystems & Nanoengineering*, Vol. 5, No. 41, 2019.
- Y. Li, H. Zhang, W. Hu et al., Fabrication and Sharpening of Silicon In-plane Microneedles with Open Capillary Networks, EIPBN 2019.

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